10/645,746

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=> d his

     (FILE 'HOME' ENTERED AT 09:14:20 ON 17 AUG 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:14:51 ON 17 AUG 2006
L1           167 S "RDE-1" OR "RDE 1"
L2         19880 S RNAI
L3           131 S L1 AND L2
L4        444660 S INTERFERENCE
L5           116 S L3 AND L4
L6            41 DUP REM L5 (75 DUPLICATES REMOVED)
L7       7844066 S CLON? OR EXPRESS? OR RECOMBINANT
L8            56 S L3 AND L7
L9            25 DUP REM L8 (31 DUPLICATES REMOVED)
                 E MELLO G C /AU
L10            6 S E3
                 E FIRE A/AU
L11          441 S E3-E7
                 E TABARA H/AU
L12          169 S E3-E6
                 E GRISHOK A/AU
L13           36 S E3
L14          620 S L10 OR L11 OR L12 OR L13
L15           39 S L3 AND L14
L16           10 DUP REM L15 (29 DUPLICATES REMOVED)
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 NEWS  4  APR 04  STN AnaVist $500 visualization usage credit offered
 NEWS  5  MAY 10  CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS  6  MAY 11  KOREAPAT updates resume
 NEWS  7  MAY 19  Derwent World Patents Index to be reloaded and enhanced
 NEWS  8  MAY 30  IPC 8 Rolled-up Core codes added to CA/CAplus and
                  USPATFULL/USPAT2
 NEWS  9  MAY 30  The F-Term thesaurus is now available in CA/CAplus
 NEWS 10  JUN 02  The first reclassification of IPC codes now complete in
                  INPADOC
 NEWS 11  JUN 26  TULSA/TULSA2 reloaded and enhanced with new search and
                  and display fields
 NEWS 12  JUN 28  Price changes in full-text patent databases EPFULL and PCTFULL
 NEWS 13  JUl 11  CHEMSAFE reloaded and enhanced
 NEWS 14  JUl 14  FSTA enhanced with Japanese patents
 NEWS 15  JUl 19  Coverage of Research Disclosure reinstated in DWPI
 NEWS 16  AUG 09  INSPEC enhanced with 1898-1968 archive

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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FILE 'HOME' ENTERED AT 09:14:20 ON 17 AUG 2006

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FILE 'LIFESCI' ENTERED AT 09:14:51 ON 17 AUG 2006
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=> s "RDE-1" or "RDE 1"
L1          167 "RDE-1" OR "RDE 1"

=> s RNAi
L2        19880 RNAI

=> s l1 and l2
L3          131 L1 AND L2

=> s interference
L4       444660 INTERFERENCE

=> s l3 and l4
L5          116 L3 AND L4

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6           41 DUP REM L5 (75 DUPLICATES REMOVED)

=> d 1-41 ibib ab

L6   ANSWER 1 OF 41  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:354964  HCAPLUS
DOCUMENT NUMBER:          145:2703
TITLE:                    Demystifying small RNA pathways meeting review
AUTHOR(S):                Pasquinelli, Amy E.
CORPORATE SOURCE:         Department of Biology, University of California, San
                          Diego, La Jolla, CA, 92093, USA
SOURCE:                   Developmental Cell (2006), 10(4), 419-424
                          CODEN: DCEEBE; ISSN: 1534-5807
PUBLISHER:                Cell Press
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review.  The Keystone Symposium entitled "RNAi and Related
     Pathways," organized by Craig Mello (University of Massachusetts), Phillip
     Zamore (University of Massachusetts) and James Carrington (Oregon State
     University), was held in Vancouver, British Columbia.  The meeting
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participants reviewed recent reports and presented new advances in our understanding of the widespread role of small noncoding RNAs in gene regulation.

L6 ANSWER 2 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:126771 HCAPLUS
DOCUMENT NUMBER: 144:249154
TITLE: Functional proteomics reveals the biochemical niche of C. elegans DCR-1 in multiple small-RNA-mediated pathways
AUTHOR(S): Duchaine, Thomas F.; Wohlschlegel, James A.; Kennedy, Scott; Bei, Yanxia; Conte, Darryl, Jr.; Pang, KaMing; Brownell, Daniel R.; Harding, Sandra; Mitani, Shohei; Ruvkun, Gary; Yates, John R., III; Mello, Craig C.
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA, 01605, USA
SOURCE: Cell (Cambridge, MA, United States) (2006), 124(2), 343-354
CODEN: CELLB5; ISSN: 0092-8674
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In plants, animals, and fungi, members of the Dicer family of RNase III-related enzymes process double-stranded RNA (dsRNA) to initiate small-RNA-mediated gene-silencing mechanisms. To learn how C. elegans Dicer, DCR-1, functions in multiple distinct silencing mechanisms, we used a mass-spectrometry-based proteomics approach to identify DCR-1-interacting proteins. We then generated and characterized deletion alleles for the corresponding genes. The interactors are required for production of three species of small RNA, including (1) small interfering RNAs (siRNAs), derived from exogenous dsRNA triggers (exo-siRNAs); (2) siRNAs derived from endogenous triggers (endo-siRNAs); and (3) developmental regulatory microRNAs (miRNAs). One interactor, the conserved RNA-phosphatase homolog PIR-1, is required for the processing of a putative amplified DCR-1 substrate. Interactors required for endo-siRNA production include ERI-1 and RRF-3, whose loss of function enhances RNAi. Our findings provide a first glimpse at the complex biochem. niche of Dicer and suggest that competition exists between DCR-1-mediated small-RNA pathways.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:15883 HCAPLUS
DOCUMENT NUMBER: 142:87587
TITLE: Mammalian embryonic stem (ES) cells having enhanced RNAi effect
INVENTOR(S): Katsuki, Motoya; Ishida, Mitsuyoshi; Kato, Minoru
PATENT ASSIGNEE(S): Mitsubishi Chemical Corporation, Japan
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of Appl. No. PCT/JP02/11831.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005003541	A1	20050106	US 2004-844406	20040513
JP 2003144141	A2	20030520	JP 2001-348705	20011114
WO 2003042382	A1	20030522	WO 2002-JP11831	20021113
W: US				

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR

PRIORITY APPLN. INFO.: JP 2001-348705 A 20011114
WO 2002-JP11831 A2 20021113

AB The object of the present invention is to provide ES cells and mammals having enhanced RNAi effect, which can be used to analyze gene functions at an individual level. The present invention provides ES cells having enhanced RNAi effect, which are obtained by performing genetic manipulation on ES cells.

L6 ANSWER 4 OF 41 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:380482 BIOSIS
DOCUMENT NUMBER: PREV200600385781
TITLE: RNAi beginnings, overview of the pathway in C-elegans.
AUTHOR(S): Grishok, Alla [Reprint Author]
CORPORATE SOURCE: MIT, Ctr Canc Res, 40 Ames St, Cambridge, MA 02139 USA
agrishok@mit.edu
SOURCE: Appasani, K [Editor]. (2005) pp. 17-28. RNA Interference Technology: From Basic Science to Drug Development. Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH ST, NEW YORK, NY 10011 USA.
ISBN: 0-521-83677-8(H).
DOCUMENT TYPE: Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Aug 2006
Last Updated on STN: 2 Aug 2006

L6 ANSWER 5 OF 41 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 2006:152965 BIOSIS
DOCUMENT NUMBER: PREV200600153005
TITLE: An antiviral role for the RNA interference machinery in Caenorhabditis elegans.
AUTHOR(S): Schott, Daniel H.; Cureton, David K.; Whelan, Sean P.; Hunter, Craig P. [Reprint Author]
CORPORATE SOURCE: Harvard Univ, Dept Mol and Cellular Biol, Cambridge, MA 02138 USA
hunter@mcb.harvard.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (DEC 20 2005) Vol. 102, No. 51, pp. 18420-18424.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Mar 2006
Last Updated on STN: 1 Mar 2006

AB RNA interference (RNAi) is a sequence-specific gene-silencing mechanism triggered by exogenous dsRNA. In plants an RNAi-like mechanism defends against viruses, but the hypothesis that animals possess a similar natural antiviral mechanism related to RNAi remains relatively untested. To test whether genes needed for RNAi defend animal cells against virus infection, we infected wild-type and RNAi-defective cells of the nematode C elegans with vesicular stomatitis virus engineered to encode a GFP fusion protein. We show that upon infection, cells lacking components of the RNAi apparatus produce more GFP and infective particles than wild-type cells. Furthermore, we show that mutant cells with enhanced RNAi produce less GFP. Our observation that multiple genes required for RNAi are also required for resistance to vesicular stomatitis virus suggests that the RNAi machinery functions in resistance to viruses in nature.

L6 ANSWER 6 OF 41 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2005441203 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16107852
TITLE: RNA interference is an antiviral defence mechanism in Caenorhabditis elegans.
AUTHOR: Wilkins Courtney; Dishongh Ryan; Moore Steve C; Whitt Michael A; Chow Marie; Machaca Khaled
CORPORATE SOURCE: Department of Microbiology, University of Arkansas for Medical Sciences, Little Rock, Arkansas 72205, USA.
SOURCE: Nature, (2005 Aug 18) Vol. 436, No. 7053, pp. 1044-7. Journal code: 0410462. E-ISSN: 1476-4687.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 19 Aug 2005
Last Updated on STN: 8 Sep 2005
Entered Medline: 7 Sep 2005

AB RNA interference (RNAi) is an evolutionarily conserved sequence-specific post-transcriptional gene silencing mechanism that is well defined genetically in Caenorhabditis elegans. RNAi has been postulated to function as an adaptive antiviral immune mechanism in the worm, but there is no experimental evidence for this. Part of the limitation is that there are no known natural viral pathogens of C. elegans. Here we describe an infection model in C. elegans using the mammalian pathogen vesicular stomatitis virus (VSV) to study the role of RNAi in antiviral immunity. VSV infection is potentiated in cells derived from RNAi-defective worm mutants (rde-1; rde-4), leading to the production of infectious progeny virus, and is inhibited in mutants with an enhanced RNAi response (rrf-3; eri-1). Because the RNAi response occurs in the absence of exogenously added VSV small interfering RNAs, these results show that RNAi is activated during VSV infection and that RNAi is a genuine antiviral immune defence mechanism in the worm.

L6 ANSWER 7 OF 41 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005441202 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16107851
TITLE: Animal virus replication and RNAi-mediated antiviral silencing in Caenorhabditis elegans.
AUTHOR: Lu R; Maduro M; Li F; Li H W; Broitman-Maduro G; Li W X; Ding S W
CORPORATE SOURCE: Institute for Integrative Genome Biology and Department of Plant Pathology, University of California, Riverside, California 92521, USA.
CONTRACT NUMBER: R01 AI052447-03 (NIAID)
SOURCE: Nature, (2005 Aug 18) Vol. 436, No. 7053, pp. 1040-3. Journal code: 0410462. E-ISSN: 1476-4687.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 19 Aug 2005
Last Updated on STN: 8 Sep 2005
Entered Medline: 7 Sep 2005

AB The worm Caenorhabditis elegans is a model system for studying many aspects of biology, including host responses to bacterial pathogens, but it is not known to support replication of any virus. Plants and insects encode multiple Dicer enzymes that recognize distinct precursors of small RNAs and may act cooperatively. However, it is not known whether the single Dicer of worms and mammals is able to initiate the small RNA-guided RNA interference (RNAi) antiviral immunity as occurs in plants and insects. Here we show complete replication of the Flock

house virus (FHV) bipartite, plus-strand RNA genome in C. elegans. We show that FHV replication in C. elegans triggers potent antiviral silencing that requires RDE-1, an Argonaute protein essential for RNAi mediated by small interfering RNAs (siRNAs) but not by microRNAs. This immunity system is capable of rapid virus clearance in the absence of FHV B2 protein, which acts as a broad-spectrum RNAi inhibitor upstream of rde-1 by targeting the siRNA precursor. This work establishes a C. elegans model for genetic studies of animal virus-host interactions and indicates that mammals might use a siRNA pathway as an antiviral response.

L6 ANSWER 8 OF 41 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2005137829 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15741313
TITLE: Transcriptional silencing of a transgene by RNAi in the soma of C. elegans.
AUTHOR: Grishok Alla; Sinskey Jina L; Sharp Phillip A
CORPORATE SOURCE: Center for Cancer Research, McGovern Institute, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA.
CONTRACT NUMBER: P01-CA42063 (NCI)
P30-CA 14051 (NCI)
R37-GM34277 (NIGMS)
SOURCE: Genes & development, (2005 Mar 15) Vol. 19, No. 6, pp. 683-96. Electronic Publication: 2005-03-01.
Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 17 Mar 2005
Last Updated on STN: 19 Apr 2005
Entered Medline: 18 Apr 2005

AB The silencing of transgene expression at the level of transcription in the soma of Caenorhabditis elegans through an RNAi-dependent pathway has not been previously characterized. Most gene silencing due to RNAi in C. elegans occurs at the post-transcriptional level. We observed transcriptional silencing when worms containing the elt-2::gfp/LacZ transgene were fed RNA produced from the commonly used L4440 vector. The transgene and the vector share plasmid backbone sequences. This transgene silencing depends on multiple RNAi pathway genes, including dcr-1, rde-1, rde-4, and rrf-1. Unlike post-transcriptional gene silencing in worms, elt-2::gfp/LacZ silencing is dependent on the PAZ-PIWI protein Alg-1 and on the HP1 homolog Hpl-2. The latter is a chromatin silencing factor, and expression of the transgene is inhibited at the level of intron-containing precursor mRNA. This inhibition is accompanied by a decrease in the acetylation of histones associated with the transgene. This transcriptional silencing in the soma can be distinguished from transgene silencing in the germline by its inability to be transmitted across generations and its dependence on the rde-1 gene. We therefore define this type of silencing as RNAi-induced Transcriptional Gene Silencing (RNAi-TGS). Additional chromatin-modifying components affecting RNAi-TGS were identified in a candidate RNAi screen.

L6 ANSWER 9 OF 41 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:229753 SCISEARCH
THE GENUINE ARTICLE: 901FC
TITLE: A member of the polymerase beta nucleotidyltransferase superfamily is required for RNA interference in C-elegans

AUTHOR: Chen C C G; Simard M J; Tabara H; Brownell D R; McCollough J A; Mello C C (Reprint)
CORPORATE SOURCE: Univ Massachusetts, Sch Med, Program Mol Med, Worcester, MA 01605 USA (Reprint); Univ Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester, MA 01605 USA; Kyoto Univ, HMRO, Grad Sch Med, Kyoto 6068501, Japan craig.mello@umassmed.edu
COUNTRY OF AUTHOR: USA; Japan
SOURCE: CURRENT BIOLOGY, (22 FEB 2005) Vol. 15, No. 4, pp. 378-383 .
ISSN: 0960-9822.
PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 20
ENTRY DATE: Entered STN: 10 Mar 2005
Last Updated on STN: 10 Mar 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB RNA interference (RNAi) is an ancient, highly conserved mechanism in which small RNA molecules (siRNAs) guide the sequence-specific silencing of gene expression [1]. Several silencing machinery protein components have been identified, including helicases, RNase-related proteins, double- and singlestranded RNA binding proteins, and RNA-dependent RNA polymerase-related proteins [2]. Work on these factors has led to the revelation that RNAi mechanisms intersect with cellular pathways required for development and fertility (3, 4]. Despite rapid progress in understanding key steps in the RNAi pathway, it is clear that many factors required for both RNAi and related developmental mechanisms have not yet been identified. Here, we report the characterization of the C. elegans gene rde-3. Genetic analysis of presumptive null alleles indicates that rde-3 is required for siRNA accumulation and for efficient RNAi in all tissues, and it is essential for fertility and viability at high temperatures. RDE-3 contains conserved domains found in the polymerase beta nucleotidyltransferase superfamily, which includes conventional poly(A) polymerases, 2'-5' oligoadenylate synthetase (OAS), and yeast Trf4p [5]. These findings implicate a new enzymatic modality in RNAi and suggest possible models for the role of RDE-3 in the RNAi mechanism.

L6 ANSWER 10 OF 41 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2005027594 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15653635
TITLE: RDE-2 interacts with MUT-7 to mediate RNA interference in Caenorhabditis elegans.
AUTHOR: Tops Bastiaan B J; Tabara Hiroaki; Sijen Titia; Simmer Femke; Mello Craig C; Plasterk Ronald H A; Ketting Rene F
CORPORATE SOURCE: Hubrecht Laboratory, Centre for Biomedical Genetics Uppsalalaan 8, 3584 CT Utrecht, The Netherlands.
SOURCE: Nucleic acids research, (2005) Vol. 33, No. 1, pp. 347-55. Electronic Publication: 2005-01-13.
Journal code: 0411011. E-ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 19 Jan 2005
Last Updated on STN: 11 Feb 2005
Entered Medline: 10 Feb 2005

AB In Caenorhabditis elegans, the activity of transposable elements is repressed in the germline. One of the mechanisms involved in this repression is RNA interference (RNAi), a process in

which dsRNA targets cleavage of mRNAs in a sequence-specific manner. The first gene found to be involved in RNAi and transposon silencing in C.elegans is mut-7, a gene encoding a putative exoribonuclease. Here, we show that the MUT-7 protein resides in complexes of approximately 250 kDa in the nucleus and in the cytosol. In addition, we find that upon triggering of RNAi the cytosolic MUT-7 complex increases in size. This increase is independent of the presence of target RNA, but does depend on the presence of RDE-1 and RDE-4, two proteins involved in small interfering RNA (siRNA) production. Finally, using a yeast two-hybrid screen, we identified RDE-2/MUT-8 as one of the other components of this complex. This protein is encoded by the rde-2/mut-8 locus, previously implicated in RNAi and transposon silencing. Using genetic complementation analysis, we show that the interaction between these two proteins is required for efficient RNAi in vivo. Together these data support a role for the MUT-7/RDE-2 complex downstream of siRNA formation, but upstream of siRNA mediated target RNA recognition, possibly indicating a role in the siRNA amplification step.

L6 ANSWER 11 OF 41 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:659496 SCISEARCH
THE GENUINE ARTICLE: 939JA
TITLE: Molecular characterization of Entamoeba histolytica RNase III and AGO2, two RNA interference hallmark proteins
AUTHOR: Abed M; Ankri S (Reprint)
CORPORATE SOURCE: Technion Israel Inst Technol, Bruce Rappaport Fac Med, Dept Mol Microbiol, POB 9649, IL-31096 Haifa, Israel (Reprint); Technion Israel Inst Technol, Bruce Rappaport Fac Med, Dept Mol Microbiol, IL-31096 Haifa, Israel sankri@tx.technion.ac.il
COUNTRY OF AUTHOR: Israel
SOURCE: EXPERIMENTAL PARASITOLOGY, (JUL 2005) Vol. 110, No. 3, pp. 265-269.
ISSN: 0014-4894.
PUBLISHER: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 19
ENTRY DATE: Entered STN: 8 Jul 2005
Last Updated on STN: 8 Jul 2005

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Entamoeba histolytica, a protozoan parasite with variable DNA content and complex ploidity, has defied most efforts aimed at gene depletion using classical genetic methods. In this study, we identified and characterized two proteins involved in the RNA interference (RNAi) pathway, RNase III and AGO2. Our results strengthen the findings that an RNAi pathway does exist in this parasite. (c) 2005 Elsevier Inc. All rights reserved.

L6 ANSWER 12 OF 41 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 6

ACCESSION NUMBER: 2004-12362 BIOTECHDS
TITLE: Inhibiting RNAi response in cell, by contacting cell with dsRNA involved in RNAi response, and inhibiting RNAi response, useful for increasing lifespan or treating premature aging in a subject who has abnormal aging disorder;
RNA interference response inhibition for use in disease therapy and gene therapy
AUTHOR: KENYON C; DILLIN A; MURPHY C
PATENT ASSIGNEE: UNIV CALIFORNIA

PATENT INFO: WO 2004029215 8 Apr 2004
APPLICATION INFO: WO 2003-US30531 26 Sep 2003
PRIORITY INFO: US 2002-413794 26 Sep 2002; US 2002-413794 26 Sep 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-305156 [28]
AB DERWENT ABSTRACT:
NOVELTY - Inhibiting (M1) an RNAi response in a cell, involves contacting the cell with a dsRNA involved in the RNAi response, thus inhibiting an RNAi response in a cell.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) inhibiting (M2) an RNAi response in a subject, involves administering a dsRNA involved in the RNAi response to the subject, thus inhibiting an RNAi response in a cell; (2) increasing (M3) lifespan or treating premature aging in a subject, involves carrying out (M2); and (3) altering (M4) lifespan regulation in a subject, involves contacting the organism with a dsRNA involved in the RNAi response, thus inhibiting an RNAi response in a cell.

BIOTECHNOLOGY - Preferred Method: In (M1), the dsRNA is a dicer (dcr-1) dsRNA, a rde-1 dsRNA, an smg-5 dsRNA, an ego-1 ds RNA, or a rde-4 ds RNA. The inhibition of the RNAi response in a cell modulates an age-associated parameter, expression of a lifespan associated gene chosen from cellular stress-response gene, an antimicrobial gene, a metabolic gene, a steroid or lipid-soluble hormone synthesis gene, a fatty acid desaturation gene or its homolog or ortholog. The inhibition of the RNAi response modulates the expression of a lifespan associated gene chosen from cytochrome P450, an estradiol-17-beta-dehydrogenase, a alcohol/short-chain dehydrogenase, an esterase, a UDP-glucuronosyltransferase, an aminopeptidase, a carboxypeptidase, an amino-oxidase, an aminoacylase, an oligopeptide transporter, metallothionein, a receptor guanylate cyclase, a mitochondrial superoxide dismutase, a catalase, lysozyme, saposin, vitellogenin, glutathione-S-transferase, heat-shock protein, heat-shock factor, an F-box/cullin/Skp protein, an isocitrate lyase, a malate synthase ASMTL, insulin, IFG1 or IFG2 or its homolog or ortholog. The dcr-1 is human dcr-1, or C. elegans dcr-1. The age-associated parameter is lifespan. The modulation is inhibition of aging. The homolog or ortholog is a human homolog or ortholog.

ACTIVITY - Dermatological; Vasotropic; Nootropic; Cytostatic.

MECHANISM OF ACTION - Inhibitor of RNAi response (claimed). The ability of dicer dsRNA to inhibit RNAi response in a cell was determined. To lower daf-2 activity during the larval stages only, wild-type animals were grown on bacteria expressing daf-2 ds RNA and then shifted to bacteria expressing dcr-1 dsRNA as day 1 adults. Control animals were grown during development on the RNAi bacteria containing the vector only and then shifted to dcr -1 RNAi bacteria as day 1 adults. Animals were grown at 25 degreesC. Daf-2 RNA was inactivated using daf-2 specific RNAi. The animals were removed from the environment RNAi stimulus (food bacteria expressing daf-2 dsRNA). The RNAi response continued to exert its effect during the adult stages and caused an increased lifespan. By shifting these animals to dcr-1RNAi in early adulthood, increased lifespan was blocked, by blocking the existing RNAi response against daf-2. In the second experiment loss of mitochondrial electron transport activity during the early development stages caused an increased adult lifespan. In contrast to the daf-2 experiment, this increased lifespan could not be reduced if the animals were shifted to dcr-1 RNAi as adults.

USE - (M1) is useful for inhibiting an RNAi response in a cell. (M2) is useful for inhibiting an RNAi response in a subject which is a mammal, preferably an adult. The mammal is a non-diabetic, non-obese adult who is not at risk for or does not have a premature aging disorder. The mammal is a healthy adult. (M3) is useful

for increasing lifespan or treating premature aging in a subject who has abnormal aging disorder such as Werner syndrome, Hutchinson-Guilford disease, Bloom's syndrome, Cockayne's syndrome, ataxia telangiectasia, and Down's syndrome (claimed).

ADMINISTRATION - The dcr-1 dsRNA is administered by parental, oral, inhalation, transdermal or rectal routes of administration. No specific dosage details are given.

EXAMPLE - Total RNA was extracted from approximately 20000 synchronized, sterile animals using trizol. Before harvest, animals were exposed to bacteria containing the RNAi vector or containing the daf-2 RNAi construct from the L1 until the L4 larval stage or from day 8 until day 10 of adulthood. Four mug of total RNA was used for one round of reverse transcription (RT) using oligo dT primers. Serial dilutions of the RT reaction (1:1-1:245) was used for PCR reaction using daf-2 specific primers. RNAi was directed to a non-overlapping 5' end of daf-2. Serial dilutions of the RT reaction (1:1-1:2) was used for PCR reaction using daf-16 specific primers. RNAi was directed to a non-overlapping 5' end of daf-16. Four mul of a 50 mul PCR reaction was analyzed on agarose gels using ethidium bromide. Wild-type hermaphrodites were allowed to lay eggs onto the control RNAi bacteria or daf-2 RNAi bacteria at 20 degreesC. The eggs were then shifted to 27 degreesC and the presence of dauer larvae were scored 48 hours later when animals would normally be reproductive adults. Lifespan, reproduction and stress assays were conducted at 20 degreesC. The total number of progeny born to a single worm over time was measured. Briefly, worms hatched within a 1 hour period was collected and allowed to develop to the L4 stage. Once in the L4 stage, worms were individually placed onto separate plates. In all cases, at least 15 worms were used for each analysis. Worms were transferred to new plates every 12 hours and the resulting progeny were allowed to grow for two days until counted for progeny measurements. The % of total progeny was calculated for each time point by dividing the number of progeny produced on a time point by the total number of progeny produced over the course of the experiment. (70 pages)

L6 ANSWER 13 OF 41 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 2004352241 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15255192
TITLE: Metalloproteases with EGF, CUB, and thrombospondin-1 domains function in molting of Caenorhabditis elegans.
AUTHOR: Suzuki Mami; Sagoh Noriko; Iwasaki Hideki; Inoue Hideshi; Takahashi Kenji
CORPORATE SOURCE: Laboratory of Molecular Biochemistry, School of Life Science, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan.
SOURCE: Biological chemistry, (2004 Jun) Vol. 385, No. 6, pp. 565-8.
Journal code: 9700112. ISSN: 1431-6730.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 17 Jul 2004
Last Updated on STN: 28 Jan 2005
Entered Medline: 27 Jan 2005

AB Functional analysis using RNAi was performed on eleven genes for metalloproteases of the M12A family in Caenorhabditis elegans and the interference of the C17G1.6 gene (nas-37) was found to cause incomplete molting. The RNAi of the C26C6.3 gene (nas-36) also caused a similar molting defect but not so severely as that of the nas-37 gene. Both the genes encode an astacin-like metalloprotease with an epidermal growth factor (EGF)-like domain, a CUB domain, and a thrombospondin-1 domain, in this order. The promoter-driven green

fluorescent protein (GFP) expression analysis suggested that they are expressed in hypodermal cells throughout the larval stages and in the vulva of adult animals. In the genetic background of rde-1(ne219), where RNAi does not work, the molting defect caused by the nas-37 interference was observed when the transgenic wild-type rde-1 gene was expressed under the control of the dpy-7 promoter, known to be active in the hypodermal cells, but not under the control of the myo-3 promoter, active in the muscular cells. Therefore these proteases are thought to be secreted by the hypodermal cells and to participate in shedding of old cuticles.

L6 ANSWER 14 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:955477 HCAPLUS
DOCUMENT NUMBER: 143:363701
TITLE: Regulation of Caenorhabditis elegans RNA interference by the daf-2 insulin stress and longevity signaling pathways
AUTHOR(S): Wang, D.; Ruvkun, G.
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital and Department of Genetics, Harvard Medical School, Boston, MA, 02114, USA
SOURCE: Cold Spring Harbor Symposia on Quantitative Biology (2004), 69, 429-431
CODEN: CSHSAZ; ISSN: 0091-7451
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study showed that Caenorhabditis elegans mutants with decreased insulin-like signaling have a more intense RNA interference (RNAi) response than wild type. Such regulation of RNAi by this stress and longevity signaling pathway suggests a role in response to pathogens such as viruses. Mutations in the insulin-like pathway enhance RNAi response and this enhancement is dependent on the DAF-16 fork head transcription factor. The insulin-like metabolic and longevity signaling is transduced by the fork head transcription factor DAF-16. One model for how insulin-like signaling affects RNAi is that components that pos. regulate RNAi, like dcr-1 and rde-1, are pos. regulated by DAF-16; or components that neg. regulate RNAi, like eri-1 and rrf-3, are neg. regulated by DAF-16.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:240580 HCAPLUS
DOCUMENT NUMBER: 141:49068
TITLE: RNA interference: a practical approach
AUTHOR(S): Duxbury, Mark S.; Whang, Edward E.
CORPORATE SOURCE: Brigham and Women's Hospital, Department of Surgery, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Journal of Surgical Research (2004), 117(2), 339-344
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Few new mol. biol. techniques have advanced to find practical application as rapidly as RNA interference (RNAi). RNAi denotes the highly specific posttranslational silencing of gene expression that occurs in response to the introduction of double-stranded RNA into a cell. The purpose of this review is to present practical guidelines for designing and executing RNAi expts. We summarize the mechanisms underlying RNAi in mammalian cells and focus on practical advice for investigators conducting RNAi expts. We suggest criteria to help select a suitable target gene

sequence, define the structural characteristics of effective siRNAs, discuss transfection strategies, and describe exptl. design, including important control methods. RNAi represents a powerful tool for determining the functions of specific genes.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 41 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 8

ACCESSION NUMBER: 2004-00966 BIOTECHDS

TITLE: Novel embryonic stem cell having increased RNA interference effect and obtained by genetically manipulating embryonic stem cells, useful for analysis of gene function in organisms;
functional genomics study involving use of transfected stem cell and transgenic animal model

PATENT ASSIGNEE: GENCOM KK

PATENT INFO: JP 2003144141 20 May 2003

APPLICATION INFO: JP 2001-348705 14 Nov 2001

PRIORITY INFO: JP 2001-348705 14 Nov 2001; JP 2001-348705 14 Nov 2001

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: WPI: 2003-818155 [77]

AB DERWENT ABSTRACT:

NOVELTY - Embryonic stem cell (I) having increased RNA interference (RNAi) effect obtained by genetically manipulating an embryonic stem cell, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a non-human mammal and its off spring derived from (I) or its part.

BIOTECHNOLOGY - Preferred Stem cell: (I) is obtained by introducing a RNAi related gene to an embryonic stem cell. The RNAi related gene is a gene which codes a factor associated with the formation of a sequence specific intermediate, a gene which codes a factor associated with target gene suppression, a gene which codes a RNA dependent RNA polymerase or a gene which codes a helicase. The RNAi related gene is preferably Nematode rde-1 or rde-4 gene, fungi qde-2 gene, Arabidopsis ago-1 gene, a dicer gene or its homolog gene which codes the protein of a PAZ/Piwi family etc., nematode Mut-7 gene, nematode rde-2, fungi qde-1 gene, nematode ego-1 gene, Arabidopsis sgs 2/sde 1 gene, fungi qde-3 gene, nematode smg-2 gene, Chlamydomonas mut 6 gene or Arabidopsis sde 3 gene, more preferably nematode rde-1 gene or Mut-7 gene. (I) is obtained by introducing a expression vector containing a RNAi related gene which can be expressed within a host cell, into an embryonic stem cell. (I) further comprises a recombinant gene (II) which contains a inverse repeat sequence of a target gene that can be expressed in a mammalian cell. (II) is present downstream of a promoter sequence functional in mammalian cell. (II) contains an enhancer sequence in the upstream of the promoter sequence, and further contains an insulator sequence or its fragment. (II) contains a poly A addition signal sequence in the downstream of the inverse repeat sequence of a target gene e.g., exogenous reporter protein or a gene encoding a variant protein. Preferably the exogenous reporter protein is enhanced green fluorescent protein (EGFP). Embryonic stem cell has an accession-number FERM P-18574 or P-18575. Preferred Mammal: The non-human mammal or its offspring is chosen from mouse, rat, hamster, guinea pig, rabbit dog, cat, horse, cow, sheep, pig, goat, and monkey.

USE - (I) is useful for analysis of gene function.

ADVANTAGE - A gene can be suppressed reliably. Related genes can be analyzed rapidly compared to the knock-out method.

EXAMPLE - A embryonic stem cell d2EGFP was established as follows. The target gene encoding enhanced green fluorescent protein (EGFP) was used to establish the stem cell d2EGFP. The d2EGFP expression vector used was pUC19 5', 3' INS24 OCE EGFP. The vector was further inserted with an

insulation sequence, a cytomegalovirus (CMV) enhances sequence and an EF-1 alpha sequence inserted to the right side of the BamH I fragment and pd2EGFP 5' INS240 CE was obtained. pd2EGFP 5' INS240 CE was digested using EcoR I and Bsa I and transfected into embryonic stem cell by electroporation method. pd2EGFP embryonic stem cell strain colony was confirmed by the EGFP fluorescence detected using a fluorescence microscope. The embryonic stem cells were cultured by standard methods. Each embryonic stem cell proliferated on the feeder cell was peeled by trypsin-EDTA and cultured in an gelatin coated plate. Then it was transfected using pUC19 5' INS240 EGFP IR having EGFP dsRNA gene containing inverse repeat sequence JP2001046089. A control was built using the plasmid with HPRT (Hypoxanthine phosphoribosyl transferase) dsRNA expression gene (inverse repeat sequence gene). The fluorescence of the cells were analyzed by FACScan. The fluorescence reduction was compared with the control which does not contain the gene. The results showed that the fluorescent reduction of the cell raises 28% compared to the control.(17 pages)

L6 ANSWER 17 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:417858 HCAPLUS
DOCUMENT NUMBER: 139:1986
TITLE: Facilitation of RNA interference (RNAi) in mammalian cell using invertebrate RNA-dependent RNA polymerase (RdRP) gene family involved in RNAi
INVENTOR(S): Mello, Craig C.; Conte, Darryl, Jr.; Chen, Chun-Chieh
PATENT ASSIGNEE(S): University of Massachusetts, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003044168	A2	20030530	WO 2002-US36725		20021115
WO 2003044168	C2	20040506			
WO 2003044168	A3	20040826			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002360394	A1	20030610	AU 2002-360394		20021115
US 2003114409	A1	20030619	US 2002-295809		20021115
PRIORITY APPLN. INFO.:			US 2001-333811P	P	20011116
			US 2001-331672P	P	20011119
			WO 2002-US36725	W	20021115

AB The present invention features compns. and methods to induce or enhance RNA interference (RNAi) in cells, systems, and organisms using mols. that mediate RNAi in invertebrates such as Caenorhabditis elegans. The invention is based, in part, on the discovery that members of the C. elegans RNA-dependent RNA polymerase (RdRP) gene family, namily ego-1 and rrf-1 genes, are involved in, and can be essential for, RNAi. Thus, RdRP expression can be used to induce or enhance RNAi in cells, including mammalian cells. RdRP genes can be expressed in combination with one or more of the other genes of the RNAi system, such as Dicer, RDE-1

, or RDE-4.

L6 ANSWER 18 OF 41 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:124284 BIOSIS
DOCUMENT NUMBER: PREV200400120663
TITLE: RNAi in Caenorhabditis elegans.
AUTHOR(S): Ketting, Rene F. [Reprint Author]; Tijsterman, Marcel [Reprint Author]; Plasterk, Ronald H. A. [Reprint Author]
CORPORATE SOURCE: Department of Functional Genomics, Hubrecht Laboratory, 3584 CT, Utrecht, Netherlands
SOURCE: Hannon, Gregory J. [Editor, Reprint Author]. (2003) pp. 65-85. RNAi: A guide to gene silencing. print.
Publisher: Cold Spring Harbor Laboratory Press, 1 Bungtown Road, P. O. Box 100, Cold Spring Harbor, NY, 11724-2203, USA.
ISBN: 0-87969-641-9 (cloth).
DOCUMENT TYPE: Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2004
Last Updated on STN: 3 Mar 2004

L6 ANSWER 19 OF 41 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003577668 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14657490
TITLE: Mutations in RNAi rescue aberrant chemotaxis of ADAR mutants.
AUTHOR: Tonkin Leath A; Bass Brenda L
CORPORATE SOURCE: Department of Biochemistry and Howard Hughes Medical Institute, University of Utah, 20 North 1900 East, Salt Lake City, UT 84132-3201, USA.
CONTRACT NUMBER: GM44073 (NIGMS)
SOURCE: Science, (2003 Dec 5) Vol. 302, No. 5651, pp. 1725.
Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 30 Dec 2003
Entered Medline: 29 Dec 2003

L6 ANSWER 20 OF 41 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:770070 SCISEARCH
THE GENUINE ARTICLE: 720HL
TITLE: Transport of dsRNA into cells by the transmembrane protein SID-1
AUTHOR: Feinberg E H; Hunter C P (Reprint)
CORPORATE SOURCE: Harvard Univ, Dept Mol & Cellular Biol, 16 Divin Ave, Cambridge, MA 02138 USA (Reprint); Harvard Univ, Dept Mol & Cellular Biol, Cambridge, MA 02138 USA
COUNTRY OF AUTHOR: USA
SOURCE: SCIENCE, (12 SEP 2003) Vol. 301, No. 5639, pp. 1545-1547.
ISSN: 0036-8075.
PUBLISHER: AMER ASSOC ADVANCEMENT SCIENCE, 1200 NEW YORK AVE, NW, WASHINGTON, DC 20005 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 21
ENTRY DATE: Entered STN: 19 Sep 2003
Last Updated on STN: 19 Sep 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB RNA interference (RNAi) spreads systemically in plants and nematodes to silence gene expression distant from the site of initiation. We previously identified a gene, sid-1, essential for systemic but not cell-autonomous RNAi in Caenorhabditis elegans. Here, we demonstrate that SID-1 is a multispan transmembrane protein that sensitizes Drosophila cells to soaking RNAi with a potency that is dependent on double-stranded RNA (dsRNA) length. Further analyses revealed that SID-1 enables passive cellular uptake of dsRNA. These data indicate that systemic RNAi in C. elegans involves SID-1-mediated intercellular transport of dsRNA.

L6 ANSWER 21 OF 41 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:682305 SCISEARCH
THE GENUINE ARTICLE: 706RN
TITLE: A gene encoding an RNase D exonuclease-like protein is required for post-transcriptional silencing in Arabidopsis
AUTHOR: Glazov E; Phillips K; Budziszewski G J; Meins F (Reprint); Levin J Z
CORPORATE SOURCE: Novartis Res Fdn, Friedrich Miescher Inst Biomed Res, Maulbeerstr 66, CH-4058 Basel, Switzerland (Reprint); Novartis Res Fdn, Friedrich Miescher Inst Biomed Res, CH-4058 Basel, Switzerland; Syngenta Biotechnol Inc, Res Triangle Pk, NC 27709 USA
COUNTRY OF AUTHOR: Switzerland; USA
SOURCE: PLANT JOURNAL, (AUG 2003) Vol. 35, No. 3, pp. 342-349. ISSN: 0960-7412.
PUBLISHER: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 43
ENTRY DATE: Entered STN: 22 Aug 2003
Last Updated on STN: 22 Aug 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Post-transcriptional gene silencing (PTGS) and the closely related phenomenon RNA interference (RNAi) result from the initial endonucleolytic cleavage of target mRNAs, which are then presumed to be completely hydrolyzed by exoribonucleases. To date, no plant genes required for PTGS are known to encode exoribonucleases. The Arabidopsis Werner Syndrome-like exonuclease (WEX) gene encodes an RNase D domain most similar to that in human Werner Syndrome protein (WRN), but lacks the RecQ helicase domain. It is also related to Caenorhabditis elegans mut-7, which is essential for RNAi, PTGS, and transposon activity. We isolated a loss-of-function mutant, wex-1, that showed greatly reduced expression of WEX mRNA and early flowering. Although wex-1 did not affect expression of a robust marker for transcriptional gene silencing (TGS), PTGS of a green-fluorescent-protein (GFP) reporter gene was blocked in wex-1 and restored by ectopic expression of WEX, indicating that WEX is required for PTGS but not TGS. Thus, members of the RNase D protein family are required for PTGS in both plants and animals. Interestingly, WEX has been shown to interact with an Arabidopsis RecQ helicase, suggesting that these proteins might comprise a functional equivalent of WRN.

L6 ANSWER 22 OF 41 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:1007849 SCISEARCH
THE GENUINE ARTICLE: 744YQ
TITLE: Transposon silencing in the Caenorhabditis elegans germ line by natural RNAi
AUTHOR: Sijen T; Plasterk R H A (Reprint)
CORPORATE SOURCE: Netherlands Inst Dev Biol, Hubrecht Lab, Uppsalalaan 8, NL-3584 CT Utrecht, Netherlands (Reprint); Netherlands

Inst Dev Biol, Hubrecht Lab, NL-3584 CT Utrecht, Netherlands
COUNTRY OF AUTHOR: Netherlands
SOURCE: NATURE, (20 NOV 2003) Vol. 426, No. 6964, pp. 310-314. ISSN: 0028-0836.
PUBLISHER: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 30
ENTRY DATE: Entered STN: 8 Dec 2003
Last Updated on STN: 8 Dec 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Transposable elements are stretches of DNA that can move and multiply within the genome of an organism. The Caenorhabditis elegans genome contains multiple Tc1 transposons that jump in somatic cells, but are silenced in the germ line(1-3). Many mutants that have lost this silencing have also lost the ability to execute RNA interference (RNAi)(2,3), a process whereby genes are suppressed by exposure to homologous double-stranded RNA (dsRNA). Here we show how RNAi causes transposon silencing in the nematode germ line. We find evidence for transposon-derived dsRNAs, in particular to the terminal inverted repeats, and show that these RNAs may derive from read-through transcription of entire transposable elements. Small interfering RNAs of Tc1 were detected. When a germline-expressed reporter gene is fused to a stretch of Tc1 sequence, this transgene is silenced in a manner dependent on functional mutator genes (mut-7, mut-16 and pk732). These results indicate that RNAi surveillance is triggered by fortuitous read-through transcription of dispersed Tc1 copies, which can form dsRNA as a result of 'snap-back' of the terminal inverted repeats. RNAi mediated by this dsRNA silences transposase gene expression.

L6 ANSWER 23 OF 41 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:932509 SCISEARCH
THE GENUINE ARTICLE: 734DD
TITLE: R2D2 leads the silencing trigger to mRNA's death star
AUTHOR: Pellino J L (Reprint); Sontheimer E J
CORPORATE SOURCE: Northwestern Univ, Dept Biochem Mol Biol & Cell Biol, Evanston, IL 60208 USA (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: CELL, (17 OCT 2003) Vol. 115, No. 2, pp. 132-133. ISSN: 0092-8674.
PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.
DOCUMENT TYPE: Editorial; Journal
LANGUAGE: English
REFERENCE COUNT: 10
ENTRY DATE: Entered STN: 7 Nov 2003
Last Updated on STN: 7 Nov 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB During RNA interference (RNAi), Dicer generates short interfering RNAs (siRNAs), which then guide target mRNA cleavage by the RISC complex. Now, Liu et al. identify R2D2, a Dicer-associated protein that is important for siRNA incorporation into RISC, thus linking the initiation and execution phases of RNAi.

L6 ANSWER 24 OF 41 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:596077 SCISEARCH
THE GENUINE ARTICLE: 696HV
TITLE: Gene silencing in Caenorhabditis elegans by transitive RNA interference
AUTHOR: Alder M N; Dames S; Gaudet J; Mango S E (Reprint)

CORPORATE SOURCE: Univ Utah, Huntsmann Canc Inst, 200 Circle Hope, Salt Lake City, UT 84112 USA (Reprint); Univ Utah, Huntsmann Canc Inst, Salt Lake City, UT 84112 USA
COUNTRY OF AUTHOR: USA
SOURCE: RNA-A PUBLICATION OF THE RNA SOCIETY, (JAN 2003) Vol. 9, No. 1, pp. 25-32.
ISSN: 1355-8382.
PUBLISHER: COLD SPRING HARBOR LAB PRESS, PUBLICATIONS DEPT, 500 SUNNYSIDE BLVD, WOODBURY, NY 11797-2924 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 56
ENTRY DATE: Entered STN: 25 Jul 2003
Last Updated on STN: 25 Jul 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB When a cell is exposed to double-stranded RNA (dsRNA), mRNA from the homologous gene is selectively degraded by a process called RNA interference (RNAi). Here, we provide evidence that dsRNA is amplified in Caenorhabditis elegans to ensure a robust RNAi response. Our data suggest a model in which mRNA targeted by RNAi functions as a template for 5' to 3' synthesis of new dsRNA (termed transitive RNAi). Strikingly, the effect is nonautonomous: dsRNA targeted to a gene expressed in one cell type can lead to transitive RNAi-mediated silencing of a second gene expressed in a distinct cell type. These data suggest dsRNA synthesized in vivo can mediate systemic RNAi.

L6 ANSWER 25 OF 41 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:602235 BIOSIS
DOCUMENT NUMBER: PREV200200602235
TITLE: The Argonaute family: Tentacles that reach into RNAi, developmental control, stem cell maintenance, and tumorigenesis.
AUTHOR(S): Carmell, Michelle A.; Xuan, Zhenyu; Zhang, Michael Q.; Hannon, Gregory J. [Reprint author]
CORPORATE SOURCE: Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 11724, USA
hannon@cshl.org
SOURCE: Genes and Development, (November 1, 2002) Vol. 16, No. 21, pp. 2733-2742. print.
CODEN: GEDEEP. ISSN: 0890-9369.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002

L6 ANSWER 26 OF 41 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2002466218 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12225671
TITLE: PPW-1, a PAZ/PIWI protein required for efficient germline RNAi, is defective in a natural isolate of C. elegans.
AUTHOR: Tijsterman Marcel; Okihara Kristy L; Thijssen Karen; Plasterk Ronald H A
CORPORATE SOURCE: Hubrecht Laboratory, Center for Biomedical Genetics, Uppsalalaan 8, 3584 CT, Utrecht, The Netherlands.
SOURCE: Current biology : CB, (2002 Sep 3) Vol. 12, No. 17, pp. 1535-40.
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 13 Sep 2002
Last Updated on STN: 17 Jun 2003
Entered Medline: 16 Jun 2003

AB One of the remarkable aspects about RNA interference (RNAi) in Caenorhabditis elegans is that the trigger molecules, dsRNA, can be administered via the animal's food. We assayed whether this feature is a universal property of the species by testing numerous strains that have been isolated from different parts of the globe. We found that one isolate from Hawaii had a defect in RNAi that was specific to the germline and was a result of multiple mutations in a PAZ/PIWI domain-containing protein, which we named PPW-1. Deleting ppw-1 in the canonical C. elegans strain Bristol N2 makes it resistant to feeding of dsRNA directed against germline-expressed genes. PPW-1 belongs to the Argonaute family of proteins, which act in posttranscriptional gene silencing and development, and is homologous to the RNAi gene rde-1. Our data indicate that at least two members of this family are required for complete and effective RNAi in C. elegans.

L6 ANSWER 27 OF 41 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2002364170 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12110183
TITLE: The dsRNA binding protein RDE-4 interacts with RDE -1, DCR-1, and a DExH-box helicase to direct RNAi in C. elegans.
AUTHOR: Tabara Hiroaki; Yigit Erbay; Siomi Haruhiko; Mello Craig C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Meidcal School, Worcester, MA 1605, USA.
CONTRACT NUMBER: GM58800 (NIGMS)
SOURCE: Cell, (2002 Jun 28) Vol. 109, No. 7, pp. 861-71. Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF480439; GENBANK-AF480440; GENBANK-AY071926
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 12 Jul 2002
Last Updated on STN: 13 Aug 2002
Entered Medline: 12 Aug 2002

AB Double-stranded (ds) RNA induces potent gene silencing, termed RNA interference (RNAi). At an early step in RNAi , an RNaseIII-related enzyme, Dicer (DCR-1), processes long-trigger dsRNA into small interfering RNAs (siRNAs). DCR-1 is also required for processing endogenous regulatory RNAs called miRNAs, but how DCR-1 recognizes its endogenous and foreign substrates is not yet understood. Here we show that the C. elegans RNAi pathway gene, rde-4, encodes a dsRNA binding protein that interacts during RNAi with RNA identical to the trigger dsRNA. RDE-4 protein also interacts in vivo with DCR-1, RDE-1, and a conserved DExH-box helicase. Our findings suggest a model in which RDE-4 and RDE-1 function together to detect and retain foreign dsRNA and to present this dsRNA to DCR-1 for processing.

L6 ANSWER 28 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:914003 HCAPLUS
DOCUMENT NUMBER: 138:333205
TITLE: RNAi and related mechanisms and their potential use for therapy
AUTHOR(S): Agami, Reuven
CORPORATE SOURCE: Division of Tumor Biology and Center for Biomedical Genetics, The Netherlands Cancer Institute, Amsterdam,

1066 CX, Neth.
SOURCE: Current Opinion in Chemical Biology (2002), 6(6), 829-834
CODEN: COCBF4; ISSN: 1367-5931
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Introduction of double-stranded RNAs into cells can suppress gene expression by mechanisms such as mRNA degradation or inhibition of translation. In mammalian cells, these two responses intersect, a feature that was recently used for the development of novel tools for stable and specific gene inactivation. These new tools were successfully applied to inhibit tumorigenicity and viral replication. Future development of appropriate in vivo delivery systems may make this technol. useful for disease therapy. Introduction of double-stranded RNAs into cells can suppress gene expression. This has recently found application in the development of novel tools for stable and specific gene inactivation. These new tools were successfully applied to inhibit tumorigenicity and viral replication.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 29 OF 41 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2002083629 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11809977
TITLE: RNA helicase MUT-14-dependent gene silencing triggered in C. elegans by short antisense RNAs.
AUTHOR: Tijsterman Marcel; Ketting Rene F; Okihara Kristy L; Sijen Titia; Plasterk Ronald H A
CORPORATE SOURCE: Hubrecht Laboratory, Center for Biomedical Genetics, Uppsalalaan 8, 3584 CT, Utrecht, Netherlands.
SOURCE: Science, (2002 Jan 25) Vol. 295, No. 5555, pp. 694-7.
Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 28 Jan 2002
Last Updated on STN: 21 Feb 2002
Entered Medline: 20 Feb 2002
AB Posttranscriptional gene silencing in Caenorhabditis elegans results from exposure to double-stranded RNA (dsRNA), a phenomenon designated as RNA interference (RNAi), or from co-suppression, in which transgenic DNA leads to silencing of both the transgene and the endogenous gene. Here we show that single-stranded RNA oligomers of antisense polarity can also be potent inducers of gene silencing. As is the case for co-suppression, antisense RNAs act independently of the RNAi genes rde-1 and rde-4 but require the mutator/RNAi gene mut-7 and a putative DEAD box RNA helicase, mut-14. Our data favor the hypothesis that gene silencing is accomplished by RNA primer extension using the mRNA as template, leading to dsRNA that is subsequently degraded.

L6 ANSWER 30 OF 41 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2002177600 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11910010
TITLE: Fertile hypomorphic ARGONAUTE (ago1) mutants impaired in post-transcriptional gene silencing and virus resistance.
AUTHOR: Morel Jean-Benoit; Godon Christian; Mourrain Philippe; Beclin Christophe; Boutet Stephanie; Feuerbach Frank; Proux Florence; Vaucheret Herve
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, Institut National de la Recherche Agronomique, 78026 Versailles Cedex, France.

SOURCE: The Plant cell, (2002 Mar) Vol. 14, No. 3, pp. 629-39.
Journal code: 9208688. ISSN: 1040-4651.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 24 Mar 2002
Last Updated on STN: 28 Jun 2002
Entered Medline: 27 Jun 2002

AB Transgene-induced post-transcriptional gene silencing (PTGS) results from specific degradation of RNAs that are homologous with the transgene transcribed sequence. This phenomenon, also known as cosuppression in plants and quelling in fungi, resembles RNA interference (RNAi) in animals. Indeed, cosuppression/quelling/RNAi require related PAZ/PIWI proteins (AGO1/QDE-2/RDE-1), indicating that these mechanisms are related. Unlike Neurospora crassa qde-2 and Caenorhabditis elegans rde-1 mutants, which are morphologically normal, the 24 known Arabidopsis ago1 mutants display severe developmental abnormalities and are sterile. Here, we report the isolation of hypomorphic ago1 mutants, including fertile ones. We show that these hypomorphic ago1 mutants are defective for PTGS, like null sgs2, sgs3, and ago1 mutants, suggesting that PTGS is more sensitive than development to perturbations in AGO1. Conversely, a mutation in ZWILLE/PINHEAD, another member of the Arabidopsis AGO1 gene family, affects development but not PTGS. Similarly, mutations in ALG-1 and ALG-2, two members of the C. elegans RDE-1 gene family, affect development but not RNAi, indicating that the control of PTGS/RNAi and development by PAZ/PIWI proteins can be uncoupled. Finally, we show that hypomorphic ago1 mutants are hypersensitive to virus infection, confirming the hypothesis that in plants PTGS is a mechanism of defense against viruses.

L6 ANSWER 31 OF 41 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2002198477 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11931230
TITLE: RNAi (Nematodes: Caenorhabditis elegans).
AUTHOR: Grishok Alla; Mello Craig C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester 01605, USA.
SOURCE: Advances in genetics, (2002) Vol. 46, pp. 339-60. Ref: 109
Journal code: 0370421. ISSN: 0065-2660.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 5 Apr 2002
Last Updated on STN: 7 Aug 2002
Entered Medline: 6 Aug 2002

AB RNA interference in Caenorhabditis elegans is a type of homology dependent posttranscriptional gene silencing induced by dsRNA. In this chapter we describe the history of the discovery of RNAi, its systemic nature, inheritance, and connection to other homology-dependent silencing phenomena like co-suppression and transcriptional gene silencing. We discuss RNAi-deficient mutants in C. elegans as well as characterized components of the RNAi, pathway, the molecular mechanism of RNAi, and its possible role in development and immunity.

L6 ANSWER 32 OF 41 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 2002120843 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11835276

TITLE: Control of developmental timing by small temporal RNAs: a paradigm for RNA-mediated regulation of gene expression.
AUTHOR: Banerjee Diya; Slack Frank
CORPORATE SOURCE: Department of Molecular, Cellular and Developmental Biology, Yale University, 266 Whitney Ave., New Haven, CT 06520, USA.
SOURCE: BioEssays : news and reviews in molecular, cellular and developmental biology, (2002 Feb) Vol. 24, No. 2, pp. 119-29. Ref: 61
Journal code: 8510851. ISSN: 0265-9247.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 22 Feb 2002
Last Updated on STN: 2 Jul 2002
Entered Medline: 1 Jul 2002

AB Heterochronic genes control the timing of developmental programs. In C. elegans, two key genes in the heterochronic pathway, lin-4 and let-7, encode small temporally expressed RNAs (stRNAs) that are not translated into protein. These stRNAs exert negative post-transcriptional regulation by binding to complementary sequences in the 3' untranslated regions of their target genes. stRNAs are transcribed as longer precursor RNAs that are processed by the RNase Dicer/DCR-1 and members of the RDE-1/AGO1 family of proteins, which are better known for their roles in RNA interference (RNAi). However, stRNA function appears unrelated to RNAi. Both sequence and temporal regulation of let-7 stRNA is conserved in other animal species suggesting that this is an evolutionarily ancient gene. Indeed, C. elegans, Drosophila and humans encode at least 86 other RNAs with similar structural features to lin-4 and let-7. We postulate that other small non-coding RNAs may function as stRNAs to control temporal identity during development in C. elegans and other organisms.

L6 ANSWER 33 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:300734 HCAPLUS
DOCUMENT NUMBER: 134:321556
TITLE: RNA interference pathway genes as tools for targeted genetic interference
INVENTOR(S): Mello, Craig C.; Fire, Andrew; Tabara, Hiroaki; Grishok, Alla
PATENT ASSIGNEE(S): University of Massachusetts, USA; Carnegie Institution of Washington
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001029058	A1	20010426	WO 2000-US28470	20001013
W: AU, CA, JP, KR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2386270	AA	20010426	CA 2000-2386270	20001013
AU 2001010865	A5	20010430	AU 2001-10865	20001013
EP 1235842	A1	20020904	EP 2000-972167	20001013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

JP 2003516124	T2	20030513	JP 2001-531856		20001013
US 2004265839	A1	20041230	US 2003-645746		20030820
US 2005100913	A1	20050512	US 2003-645735		20030820
US 2006024798	A1	20060202	US 2005-144985		20050603
AU 2006201716	A1	20060525	AU 2006-201716		20060426
PRIORITY APPLN. INFO.:			US 1999-159776P	P	19991015
			US 2000-193218P	P	20000330
			AU 2001-10865	A3	20001013
			US 2000-689992	A3	20001013
			WO 2000-US28470	W	20001013

AB Genes involved in double-stranded RNA interference (RNAi pathway genes) are identified and used to investigate the RNAi pathway. RNAi pathway components provide activities necessary for double-stranded RNA-dependent gene silencing (genetic interference). Genes RDE-1 and RDE-4 were identified using screens for Caenorhabditis elegans strains mutant for RNAi, and the mutations are further characterized for germline and somatic effects, effects on transposon mobilization, X chromosome loss and transgene silencing, and target tissue activity. The genes and their products are also useful for modulating RNAi pathway activity.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 34 OF 41 MEDLINE on STN DUPLICATE 16

ACCESSION NUMBER: 2001574258 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11680844
TITLE: Distinct roles for RDE-1 and RDE-4 during RNA interference in Caenorhabditis elegans.
AUTHOR: Parrish S; Fire A
CORPORATE SOURCE: Department of Embryology, Carnegie Institution of Washington, Baltimore, Maryland 21210, USA.
CONTRACT NUMBER: GM07231 (NIGMS)
GM37706 (NIGMS)
SOURCE: RNA (New York, N.Y.), (2001 Oct) Vol. 7, No. 10, pp. 1397-402.
Journal code: 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 30 Oct 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 4 Dec 2001

AB RNA interference (RNAi) is a cellular defense mechanism that uses double-stranded RNA (dsRNA) as a sequence-specific trigger to guide the degradation of homologous single-stranded RNAs. RNAi is a multistep process involving several proteins and at least one type of RNA intermediate, a population of small 21-25 nt RNAs (called siRNAs) that are initially derived from cleavage of the dsRNA trigger. Genetic screens in Caenorhabditis elegans have identified numerous mutations that cause partial or complete loss of RNAi. In this work, we analyzed cleavage of injected dsRNA to produce the initial siRNA population in animals mutant for rde-1 and rde-4, two genes that are essential for RNAi but that are not required for organismal viability or fertility. Our results suggest distinct roles for RDE-1 and RDE-4 in the interference process. Although null mutants lacking rde -1 show no phenotypic response to dsRNA, the amount of siRNAs generated from an injected dsRNA trigger was comparable to that of wild-type. By contrast, mutations in rde-4 substantially reduced the population of siRNAs derived from an injected dsRNA trigger. Injection of chemically synthesized 24- or 25-nt siRNAs could circumvent RNAi

resistance in rde-4 mutants, whereas no bypass was observed in rde -1 mutants. These results support a model in which RDE-4 is involved before or during production of siRNAs, whereas RDE-1 acts after the siRNAs have been formed.

L6 ANSWER 35 OF 41 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 2001412025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11461699
TITLE: Genes and mechanisms related to RNA interference regulate expression of the small temporal RNAs that control C. elegans developmental timing.
AUTHOR: Grishok A; Pasquinelli A E; Conte D; Li N; Parrish S; Ha I; Baillie D L; Fire A; Ruvkun G; Mello C C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA.
CONTRACT NUMBER: GM07321 (NIGMS)
GM37706 (NIGMS)
GM58800 (NIGMS)
SOURCE: Cell, (2001 Jul 13) Vol. 106, No. 1, pp. 23-34.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 13 Aug 2001
Last Updated on STN: 13 Aug 2001
Entered Medline: 9 Aug 2001
AB RNAi is a gene-silencing phenomenon triggered by double-stranded (ds) RNA and involves the generation of 21 to 26 nt RNA segments that guide mRNA destruction. In Caenorhabditis elegans, lin-4 and let-7 encode small temporal RNAs (stRNAs) of 22 nt that regulate stage-specific development. Here we show that inactivation of genes related to RNAi pathway genes, a homolog of Drosophila Dicer (dcr-1), and two homologs of rde-1 (alg-1 and alg-2), cause heterochronic phenotypes similar to lin-4 and let-7 mutations. Further we show that dcr-1, alg-1, and alg-2 are necessary for the maturation and activity of the lin-4 and let-7 stRNAs. Our findings suggest that a common processing machinery generates guide RNAs that mediate both RNAi and endogenous gene regulation.

L6 ANSWER 36 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2000207007 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10741970
TITLE: Genetic requirements for inheritance of RNAi in C. elegans.
AUTHOR: Grishok A; Tabara H; Mello C C
CORPORATE SOURCE: Program in Molecular Medicine, Department of Cell Biology, University of Massachusetts Cancer Center, Two Biotech Suite 213, 373 Plantation Street, Worcester, MA 01605, USA.
CONTRACT NUMBER: GM58800 (NIGMS)
SOURCE: Science, (2000 Mar 31) Vol. 287, No. 5462, pp. 2494-7.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000
Entered Medline: 11 Apr 2000
AB In Caenorhabditis elegans, the introduction of double-stranded RNA triggers sequence-specific genetic interference (RNAi)

that is transmitted to offspring. The inheritance properties associated with this phenomenon were examined. Transmission of the interference effect occurred through a dominant extragenic agent. The wild-type activities of the RNAi pathway genes rde -1 and rde-4 were required for the formation of this interfering agent but were not needed for interference thereafter. In contrast, the rde-2 and mut-7 genes were required downstream for interference. These findings provide evidence for germ line transmission of an extragenic sequence-specific silencing factor and implicate rde-1 and rde-4 in the formation of the inherited agent.

L6 ANSWER 37 OF 41 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 2001022703 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11016954
TITLE: AGO1, QDE-2, and RDE-1 are related proteins required for post-transcriptional gene silencing in plants, quelling in fungi, and RNA interference in animals.
AUTHOR: Fagard M; Boutet S; Morel J B; Bellini C; Vaucheret H
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, Institut National de la Recherche Agronomique, 78026 Versailles Cedex, France.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2000 Oct 10) Vol. 97, No. 21, pp. 11650-4.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 9 Nov 2000
AB Introduction of transgene DNA may lead to specific degradation of RNAs that are homologous to the transgene transcribed sequence through phenomena named post-transcriptional gene silencing (PTGS) in plants, quelling in fungi, and RNA interference (RNAi) in animals. It was shown previously that PTGS, quelling, and RNAi require a set of related proteins (SGS2, QDE-1, and EGO-1, respectively). Here we report the isolation of Arabidopsis mutants impaired in PTGS which are affected at the Argonaute1 (AGO1) locus. AGO1 is similar to QDE-2 required for quelling and RDE-1 required for RNAi. Sequencing of ago1 mutants revealed one amino acid essential for PTGS that is also present in QDE-2 and RDE-1 in a highly conserved motif. Taken together, these results confirm the hypothesis that these processes derive from a common ancestral mechanism that controls expression of invading nucleic acid molecules at the post-transcriptional level. As opposed to rde-1 and qde-2 mutants, which are viable, ago1 mutants display several developmental abnormalities, including sterility. These results raise the possibility that PTGS, or at least some of its elements, could participate in the regulation of gene expression during development in plants.

L6 ANSWER 38 OF 41 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 19
ACCESSION NUMBER: 2000123929 EMBASE
TITLE: Genetic requirements for inheritance of RNAi in C. elegans.
AUTHOR: Grishok A.; Tabara H.; Mello C.C.
CORPORATE SOURCE: C.C. Mello, Program in Molecular Medicine, Department of Cell Biology, Univ. of Massachusetts Cancer Center, 373 Plantation Street, Worcester, MA 01605, United States. craig.mello@ummed.edu

SOURCE: Science, (31 Mar 2000) Vol. 287, No. 5462, pp. 2494-2497. .
ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000

AB In Caenorhabditis elegans, the introduction of double-stranded RNA triggers sequence-specific genetic interference (RNAi) that is transmitted to offspring. The inheritance properties associated with this phenomenon were examined. Transmission of the interference effect occurred through a dominant extragenic agent. The wild-type activities of the RNAi pathway genes rde -1 and rde-4 were required for the formation of this interfering agent but were not needed for interference thereafter. In contrast, the rde-2 and mut-7 genes were required downstream for interference. These findings provide evidence for germ line transmission of an extragenic sequence-specific silencing factor and implicate rde-1 and rde-4 in the formation of the inherited agent.

L6 ANSWER 39 OF 41 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:535206 SCISEARCH
THE GENUINE ARTICLE: 333TC
TITLE: Transgene-mediated cosuppression in the C-elegans germ line
AUTHOR: Dernburg A F; Zalevsky J; Colaiacovo M P; Villeneuve A M (Reprint)
CORPORATE SOURCE: Stanford Univ, Sch Med, Dept Dev Biol, Stanford, CA 94305 USA (Reprint); Stanford Univ, Sch Med, Dept Genet, Stanford, CA 94305 USA
COUNTRY OF AUTHOR: USA
SOURCE: GENES & DEVELOPMENT, (1 JUL 2000) Vol. 14, No. 13, pp. 1578-1583.
ISSN: 0890-9369.
PUBLISHER: COLD SPRING HARBOR LAB PRESS, 1 BUNGTOWN RD, PLAINVIEW, NY 11724 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 40
ENTRY DATE: Entered STN: 2000
Last Updated on STN: 2000
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Functional silencing of chromosomal loci can be induced by transgenes (cosuppression) or by introduction of double-stranded RNA (RNAi). Here, we demonstrate the generality of and define rules for a transgene-mediated cosuppression phenomenon in the Caenorhabditis elegans germ line. Functional repression is not a consequence of persistent physical association between transgenes and endogenous genes or of mutations in affected genes. The cosuppression mechanism likely involves an RNA mediator that defines its target specificity, reminiscent of RNAi. Cosuppression is strongly abrogated in rde-2 and mut-7 mutants, but is not blocked in an rde-1 mutant, indicating that cosuppression and RNAi have overlapping but distinct genetic requirements.

L6 ANSWER 40 OF 41 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:156834 HCAPLUS
DOCUMENT NUMBER: 132:343839
TITLE: Gene silencing: shrinking the black box of RNAi

AUTHOR(S): Hunter, Craig P.
CORPORATE SOURCE: Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Current Biology (2000), 10(4), R137-R140
CODEN: CUBLE2; ISSN: 0960-9822
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 25 refs. The mysterious mechanism whereby the mere presence of double-stranded RNA can inactivate specific genes is yielding its secrets. Recent results identifying cellular components required for RNAi (RNA interference) in Caenorhabditis elegans indicate that the mechanism is conserved, ancient and may provide a defense against selfish DNA.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 41 OF 41 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 2000004389 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10535731
TITLE: The rde-1 gene, RNA interference, and transposon silencing in C. elegans.
AUTHOR: Tabara H; Sarkissian M; Kelly W G; Fleenor J; Grishok A; Timmons L; Fire A; Mello C C
CORPORATE SOURCE: Department of Cell Biology, Program in Molecular Medicine, University of Massachusetts Cancer Center, Worcester 01605, USA.
CONTRACT NUMBER: GM37706 (NIGMS)
GM58800 (NIGMS)
HD08353 (NICHD)
SOURCE: Cell, (1999 Oct 15) Vol. 99, No. 2, pp. 123-32.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF180730
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 10 Nov 1999
AB Double-stranded (ds) RNA can induce sequence-specific inhibition of gene function in several organisms. However, both the mechanism and the physiological role of the interference process remain mysterious. In order to study the interference process, we have selected C. elegans mutants resistant to dsRNA-mediated interference (RNAi). Two loci, rde-1 and rde-4, are defined by mutants strongly resistant to RNAi but with no obvious defects in growth or development. We show that rde-1 is a member of the piwi/sting/argonaute/zwille/eIF 2C gene family conserved from plants to vertebrates. Interestingly, several, but not all, RNAi-deficient strains exhibit mobilization of the endogenous transposons. We discuss implications for the mechanism of RNAi and the possibility that one natural function of RNAi is transposon silencing.

=> s clon? or express? or recombinant
L7 7844066 CLON? OR EXPRESS? OR RECOMBINANT

=> d his

(FILE 'HOME' ENTERED AT 09:14:20 ON 17 AUG 2006)

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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:14:51 ON 17 AUG 2006
L1           167 S "RDE-1" OR "RDE 1"
L2         19880 S RNAI
L3           131 S L1 AND L2
L4        444660 S INTERFERENCE
L5           116 S L3 AND L4
L6            41 DUP REM L5 (75 DUPLICATES REMOVED)
L7       7844066 S CLON? OR EXPRESS? OR RECOMBINANT

=> s l3 and l7
L8           56 L3 AND L7

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9            25 DUP REM L8 (31 DUPLICATES REMOVED)

=> d 1-25 ibib ab

L9   ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:15883  HCAPLUS
DOCUMENT NUMBER:          142:87587
TITLE:                    Mammalian embryonic stem (ES) cells having enhanced
                          RNAi effect
INVENTOR(S):              Katsuki, Motoya; Ishida, Mitsuyoshi; Kato, Minoru
PATENT ASSIGNEE(S):       Mitsubishi Chemical Corporation, Japan
SOURCE:                   U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of Appl.
                          No. PCT/JP02/11831.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 2005003541         A1    20050106    US 2004-844406          20040513
     JP 2003144141         A2    20030520    JP 2001-348705          20011114
     WO 2003042382         A1    20030522    WO 2002-JP11831         20021113
         W:  US
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, SK, TR
PRIORITY APPLN. INFO.:                       JP 2001-348705      A  20011114
                                             WO 2002-JP11831     A2 20021113
AB   The object of the present invention is to provide ES cells and mammals
     having enhanced RNAi effect, which can be used to analyze gene
     functions at an individual level.  The present invention provides ES cells
     having enhanced RNAi effect, which are obtained by performing
     genetic manipulation on ES cells.

L9   ANSWER 2 OF 25     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2005441202     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 16107851
TITLE:              Animal virus replication and RNAi-mediated
                    antiviral silencing in Caenorhabditis elegans.
AUTHOR:             Lu R; Maduro M; Li F; Li H W; Broitman-Maduro G; Li W X;
                    Ding S W
CORPORATE SOURCE:   Institute for Integrative Genome Biology and Department of
                    Plant Pathology, University of California, Riverside,
                    California 92521, USA.
CONTRACT NUMBER:    R01 AI052447-03 (NIAID)
SOURCE:             Nature, (2005 Aug 18) Vol. 436, No. 7053, pp. 1040-3.
                    Journal code: 0410462. E-ISSN: 1476-4687.
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PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 19 Aug 2005
Last Updated on STN: 8 Sep 2005
Entered Medline: 7 Sep 2005

AB The worm Caenorhabditis elegans is a model system for studying many aspects of biology, including host responses to bacterial pathogens, but it is not known to support replication of any virus. Plants and insects encode multiple Dicer enzymes that recognize distinct precursors of small RNAs and may act cooperatively. However, it is not known whether the single Dicer of worms and mammals is able to initiate the small RNA-guided RNA interference (RNAi) antiviral immunity as occurs in plants and insects. Here we show complete replication of the Flock house virus (FHV) bipartite, plus-strand RNA genome in C. elegans. We show that FHV replication in C. elegans triggers potent antiviral silencing that requires RDE-1, an Argonaute protein essential for RNAi mediated by small interfering RNAs (siRNAs) but not by microRNAs. This immunity system is capable of rapid virus clearance in the absence of FHV B2 protein, which acts as a broad-spectrum RNAi inhibitor upstream of rde-1 by targeting the siRNA precursor. This work establishes a C. elegans model for genetic studies of animal virus-host interactions and indicates that mammals might use a siRNA pathway as an antiviral response.

L9 ANSWER 3 OF 25 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005137829 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15741313
TITLE: Transcriptional silencing of a transgene by RNAi in the soma of C. elegans.
AUTHOR: Grishok Alla; Sinskey Jina L; Sharp Phillip A
CORPORATE SOURCE: Center for Cancer Research, McGovern Institute, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA.
CONTRACT NUMBER: P01-CA42063 (NCI)
P30-CA 14051 (NCI)
R37-GM34277 (NIGMS)
SOURCE: Genes & development, (2005 Mar 15) Vol. 19, No. 6, pp. 683-96. Electronic Publication: 2005-03-01.
Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 17 Mar 2005
Last Updated on STN: 19 Apr 2005
Entered Medline: 18 Apr 2005

AB The silencing of transgene expression at the level of transcription in the soma of Caenorhabditis elegans through an RNAi-dependent pathway has not been previously characterized. Most gene silencing due to RNAi in C. elegans occurs at the post-transcriptional level. We observed transcriptional silencing when worms containing the elt-2::gfp/LacZ transgene were fed RNA produced from the commonly used L4440 vector. The transgene and the vector share plasmid backbone sequences. This transgene silencing depends on multiple RNAi pathway genes, including dcr-1, rde-1, rde-4, and rrf-1. Unlike post-transcriptional gene silencing in worms, elt-2::gfp/LacZ silencing is dependent on the PAZ-PIWI protein Alg-1 and on the HP1 homolog Hpl-2. The latter is a chromatin silencing factor, and expression of the transgene is inhibited at the level of intron-containing precursor mRNA. This inhibition is accompanied by a

decrease in the acetylation of histones associated with the transgene. This transcriptional silencing in the soma can be distinguished from transgene silencing in the germline by its inability to be transmitted across generations and its dependence on the rde-1 gene. We therefore define this type of silencing as RNAi -induced Transcriptional Gene Silencing (RNAi-TGS). Additional chromatin-modifying components affecting RNAi-TGS were identified in a candidate RNAi screen.

L9 ANSWER 4 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:229753 SCISEARCH
THE GENUINE ARTICLE: 901FC
TITLE: A member of the polymerase beta nucleotidyltransferase superfamily is required for RNA interference in C-elegans
AUTHOR: Chen C C G; Simard M J; Tabara H; Brownell D R; McCollough J A; Mello C C (Reprint)
CORPORATE SOURCE: Univ Massachusetts, Sch Med, Program Mol Med, Worcester, MA 01605 USA (Reprint); Univ Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester, MA 01605 USA; Kyoto Univ, HMRO, Grad Sch Med, Kyoto 6068501, Japan craig.mello@umassmed.edu
COUNTRY OF AUTHOR: USA; Japan
SOURCE: CURRENT BIOLOGY, (22 FEB 2005) Vol. 15, No. 4, pp. 378-383.
ISSN: 0960-9822.
PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 20
ENTRY DATE: Entered STN: 10 Mar 2005
Last Updated on STN: 10 Mar 2005

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB RNA interference (RNAi) is an ancient, highly conserved mechanism in which small RNA molecules (siRNAs) guide the sequence-specific silencing of gene expression [1]. Several silencing machinery protein components have been identified, including helicases, RNase-related proteins, double- and singlestranded RNA binding proteins, and RNA-dependent RNA polymerase-related proteins [2]. Work on these factors has led to the revelation that RNAi mechanisms intersect with cellular pathways required for development and fertility (3, 4]. Despite rapid progress in understanding key steps in the RNAi pathway, it is clear that many factors required for both RNAi and related developmental mechanisms have not yet been identified. Here, we report the characterization of the C. elegans gene rde-3. Genetic analysis of presumptive null alleles indicates that rde-3 is required for siRNA accumulation and for efficient RNAi in all tissues, and it is essential for fertility and viability at high temperatures. RDE-3 contains conserved domains found in the polymerase beta nucleotidyltransferase superfamily, which includes conventional poly(A) polymerases, 2'-5' oligoadenylate synthetase (OAS), and yeast Trf4p [5]. These findings implicate a new enzymatic modality in RNAi and suggest possible models for the role of RDE-3 in the RNAi mechanism.

L9 ANSWER 5 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:659496 SCISEARCH
THE GENUINE ARTICLE: 939JA
TITLE: Molecular characterization of Entamoeba histolytica RNase III and AGO2, two RNA interference hallmark proteins
AUTHOR: Abed M; Ankri S (Reprint)
CORPORATE SOURCE: Technion Israel Inst Technol, Bruce Rappaport Fac Med,

Dept Mol Microbiol, POB 9649, IL-31096 Haifa, Israel (Reprint); Technion Israel Inst Technol, Bruce Rappaport Fac Med, Dept Mol Microbiol, IL-31096 Haifa, Israel sankri@tx.technion.ac.il
COUNTRY OF AUTHOR: Israel
SOURCE: EXPERIMENTAL PARASITOLOGY, (JUL 2005) Vol. 110, No. 3, pp. 265-269.
ISSN: 0014-4894.
PUBLISHER: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 19
ENTRY DATE: Entered STN: 8 Jul 2005
Last Updated on STN: 8 Jul 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Entamoeba histolytica, a protozoan parasite with variable DNA content and complex ploidity, has defied most efforts aimed at gene depletion using classical genetic methods. In this study, we identified and characterized two proteins involved in the RNA interference (RNAi) pathway, RNase III and AGO2. Our results strengthen the findings that an RNAi pathway does exist in this parasite. (c) 2005 Elsevier Inc. All rights reserved.

ACCESSION NUMBER: 2004-12362 BIOTECHDS
TITLE: Inhibiting RNAi response in cell, by contacting cell with dsRNA involved in RNAi response, and inhibiting RNAi response, useful for increasing lifespan or treating premature aging in a subject who has abnormal aging disorder;
RNA interference response inhibition for use in disease therapy and gene therapy
AUTHOR: KENYON C; DILLIN A; MURPHY C
PATENT ASSIGNEE: UNIV CALIFORNIA
PATENT INFO: WO 2004029215 8 Apr 2004
APPLICATION INFO: WO 2003-US30531 26 Sep 2003
PRIORITY INFO: US 2002-413794 26 Sep 2002; US 2002-413794 26 Sep 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-305156 [28]

AB DERWENT ABSTRACT:
NOVELTY - Inhibiting (M1) an RNAi response in a cell, involves contacting the cell with a dsRNA involved in the RNAi response, thus inhibiting an RNAi response in a cell.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) inhibiting (M2) an RNAi response in a subject, involves administering a dsRNA involved in the RNAi response to the subject, thus inhibiting an RNAi response in a cell; (2) increasing (M3) lifespan or treating premature aging in a subject, involves carrying out (M2); and (3) altering (M4) lifespan regulation in a subject, involves contacting the organism with a dsRNA involved in the RNAi response, thus inhibiting an RNAi response in a cell.
BIOTECHNOLOGY - Preferred Method: In (M1), the dsRNA is a dicer (dcr-1) dsRNA, a rde-1 dsRNA, an smg-5 dsRNA, an ego-1 ds RNA, or a rde-4 ds RNA. The inhibition of the RNAi response in a cell modulates an age-associated parameter, expression of a lifespan associated gene chosen from cellular stress-response gene, an antimicrobial gene, a metabolic gene, a steroid or lipid-soluble hormone synthesis gene, a fatty acid desaturation gene or its homolog or ortholog. The inhibition of the RNAi response modulates the expression of a lifespan associated gene chosen

from cytochrome P450, an estradiol-17-beta-dehydrogenase, a alcohol/short-chain dehydrogenase, an esterase, a UDP-glucuronosyltransferase, an aminopeptidase, a carboxypeptidase, an amino-oxidase, an aminoacylase, an oligopeptide transporter, metallothionein, a receptor guanylate cyclase, a mitochondrial superoxide dismutase, a catalase, lysozyme, saposin, vitellogenin, glutathione-S-transferase, heat-shock protein, heat-shock factor, an F-box/cullin/Skp protein, an isocitrate lyase, a malate synthase ASMTL, insulin, IFG1 or IFG2 or its homolog or ortholog. The dcr-1 is human dcr-1, or C. elegans dcr-1. The age-associated parameter is lifespan. The modulation is inhibition of aging. The homolog or ortholog is a human homolog or ortholog.

ACTIVITY - Dermatological; Vasotropic; Nootropic; Cytostatic.

MECHANISM OF ACTION - Inhibitor of RNAi response (claimed). The ability of dicer dsRNA to inhibit RNAi response in a cell was determined. To lower daf-2 activity during the larval stages only, wild-type animals were grown on bacteria expressing daf-2 ds RNA and then shifted to bacteria expressing dcr-1 dsRNA as day 1 adults. Control animals were grown during development on the RNAi bacteria containing the vector only and then shifted to dcr -1 RNAi bacteria as day 1 adults. Animals were grown at 25 degreesC. Daf-2 RNA was inactivated using daf-2 specific RNAi . The animals were removed from the environment RNAi stimulus (food bacteria expressing daf-2 dsRNA). The RNAi response continued to exert its effect during the adult stages and caused an increased lifespan. By shifting these animals to dcr-1RNAi in early adulthood, increased lifespan was blocked, by blocking the existing RNAi response against daf-2. In the second experiment loss of mitochondrial electron transport activity during the early development stages caused an increased adult lifespan. In contrast to the daf-2 experiment, this increased lifespan could not be reduced if the animals were shifted to dcr-1 RNAi as adults.

USE - (M1) is useful for inhibiting an RNAi response in a cell. (M2) is useful for inhibiting an RNAi response in a subject which is a mammal, preferably an adult. The mammal is a non-diabetic, non-obese adult who is not at risk for or does not have a premature aging disorder. The mammal is a healthy adult. (M3) is useful for increasing lifespan or treating premature aging in a subject who has abnormal aging disorder such as Werner syndrome, Hutchinson-Guilford disease, Bloom's syndrome, Cockayne's syndrome, ataxia telangiectasia, and Down's syndrome (claimed).

ADMINISTRATION - The dcr-1 dsRNA is administered by parental, oral, inhalation, transdermal or rectal routes of administration. No specific dosage details are given.

EXAMPLE - Total RNA was extracted from approximately 20000 synchronized, sterile animals using trizol. Before harvest, animals were exposed to bacteria containing the RNAi vector or containing the daf-2 RNAi construct from the L1 until the L4 larval stage or from day 8 until day 10 of adulthood. Four mug of total RNA was used for one round of reverse transcription (RT) using oligo dT primers. Serial dilutions of the RT reaction (1:1-1:245) was used for PCR reaction using daf-2 specific primers. RNAi was directed to a non-overlapping 5' end of daf-2. Serial dilutions of the RT reaction (1:1-1:2) was used for PCR reaction using daf-16 specific primers. RNAi was directed to a non-overlapping 5' end of daf-16. Four mul of a 50 mul PCR reaction was analyzed on agarose gels using ethidium bromide. Wild-type hermaphrodites were allowed to lay eggs onto the control RNAi bacteria or daf-2 RNAi bacteria at 20 degreesC. The eggs were then shifted to 27 degreesC and the presence of dauer larvae were scored 48 hours later when animals would normally be reproductive adults. Lifespan, reproduction and stress assays were conducted at 20 degreesC. The total number of progeny born to a single worm over time was measured. Briefly, worms hatched within a 1 hour period was collected and allowed to develop to the L4 stage. Once in the

L4 stage, worms were individually placed onto separate plates. In all cases, at least 15 worms were used for each analysis. Worms were transferred to new plates every 12 hours and the resulting progeny were allowed to grow for two days until counted for progeny measurements. The % of total progeny was calculated for each time point by dividing the number of progeny produced on a time point by the total number of progeny produced over the course of the experiment. (70 pages)

L9 ANSWER 7 OF 25 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004352241 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15255192
TITLE: Metalloproteases with EGF, CUB, and thrombospondin-1 domains function in molting of Caenorhabditis elegans.
AUTHOR: Suzuki Mami; Sagoh Noriko; Iwasaki Hideki; Inoue Hideshi; Takahashi Kenji
CORPORATE SOURCE: Laboratory of Molecular Biochemistry, School of Life Science, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan.
SOURCE: Biological chemistry, (2004 Jun) Vol. 385, No. 6, pp. 565-8.
Journal code: 9700112. ISSN: 1431-6730.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 17 Jul 2004
Last Updated on STN: 28 Jan 2005
Entered Medline: 27 Jan 2005

AB Functional analysis using RNAi was performed on eleven genes for metalloproteases of the M12A family in Caenorhabditis elegans and the interference of the C17G1.6 gene (nas-37) was found to cause incomplete molting. The RNAi of the C26C6.3 gene (nas-36) also caused a similar molting defect but not so severely as that of the nas-37 gene. Both the genes encode an astacin-like metalloprotease with an epidermal growth factor (EGF)-like domain, a CUB domain, and a thrombospondin-1 domain, in this order. The promoter-driven green fluorescent protein (GFP) expression analysis suggested that they are expressed in hypodermal cells throughout the larval stages and in the vulva of adult animals. In the genetic background of rde-1(ne219), where RNAi does not work, the molting defect caused by the nas-37 interference was observed when the transgenic wild-type rde-1 gene was expressed under the control of the dpy-7 promoter, known to be active in the hypodermal cells, but not under the control of the myo-3 promoter, active in the muscular cells. Therefore these proteases are thought to be secreted by the hypodermal cells and to participate in shedding of old cuticles.

L9 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:240580 HCAPLUS
DOCUMENT NUMBER: 141:49068
TITLE: RNA interference: a practical approach
AUTHOR(S): Duxbury, Mark S.; Whang, Edward E.
CORPORATE SOURCE: Brigham and Women's Hospital, Department of Surgery, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Journal of Surgical Research (2004), 117(2), 339-344
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Few new mol. biol. techniques have advanced to find practical application as rapidly as RNA interference (RNAi). RNAi denotes the highly specific posttranslational silencing of gene expression that occurs in response to the introduction of

double-stranded RNA into a cell. The purpose of this review is to present practical guidelines for designing and executing RNAi expts. We summarize the mechanisms underlying RNAi in mammalian cells and focus on practical advice for investigators conducting RNAi expts. We suggest criteria to help select a suitable target gene sequence, define the structural characteristics of effective siRNAs, discuss transfection strategies, and describe exptl. design, including important control methods. RNAi represents a powerful tool for determining the functions of specific genes.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 25 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 5

ACCESSION NUMBER: 2004-00966 BIOTECHDS

TITLE: Novel embryonic stem cell having increased RNA interference effect and obtained by genetically manipulating embryonic stem cells, useful for analysis of gene function in organisms ;

functional genomics study involving use of transfected stem cell and transgenic animal model

PATENT ASSIGNEE: GENCOM KK

PATENT INFO: JP 2003144141 20 May 2003

APPLICATION INFO: JP 2001-348705 14 Nov 2001

PRIORITY INFO: JP 2001-348705 14 Nov 2001; JP 2001-348705 14 Nov 2001

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: WPI: 2003-818155 [77]

AB DERWENT ABSTRACT:

NOVELTY - Embryonic stem cell (I) having increased RNA interference (RNAi) effect obtained by genetically manipulating an embryonic stem cell, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a non-human mammal and its off spring derived from (I) or its part.

BIOTECHNOLOGY - Preferred Stem cell: (I) is obtained by introducing a RNAi related gene to an embryonic stem cell. The RNAi related gene is a gene which codes a factor associated with the formation of a sequence specific intermediate, a gene which codes a factor associated with target gene suppression, a gene which codes a RNA dependent RNA polymerase or a gene which codes a helicase. The RNAi related gene is preferably Nematode rde-1 or rde-4 gene, fungi qde-2 gene, Arabidopsis ago-1 gene, a dicer gene or its homolog gene which codes the protein of a PAZ/Piwi family etc., nematode Mut-7 gene, nematode rde-2, fungi qde-1 gene, nematode ego-1 gene, Arabidopsis sgs 2/sde 1 gene, fungi qde-3 gene, nematode smg-2 gene, Chlamydomonas mut 6 gene or Arabidopsis sde 3 gene, more preferably nematode rde-1 gene or Mut-7 gene. (I) is obtained by introducing a expression vector containing a RNAi related gene which can be expressed within a host cell, into an embryonic stem cell. (I) further comprises a recombinant gene (II) which contains a inverse repeat sequence of a target gene that can be expressed in a mammalian cell. (II) is present downstream of a promoter sequence functional in mammalian cell. (II) contains an enhancer sequence in the upstream of the promoter sequence, and further contains an insulator sequence or its fragment. (II) contains a poly A addition signal sequence in the downstream of the inverse repeat sequence of a target gene e.g., exogenous reporter protein or a gene encoding a variant protein. Preferably the exogenous reporter protein is enhanced green fluorescent protein (EGFP). Embryonic stem cell has an accession-number FERM P-18574 or P-18575. Preferred Mammal: The non-human mammal or its offspring is chosen from mouse, rat, hamster, guinea pig, rabbit dog, cat, horse, cow, sheep, pig, goat, and monkey.

USE - (I) is useful for analysis of gene function.

ADVANTAGE - A gene can be suppressed reliably. Related genes can be

analyzed rapidly compared to the knock-out method.

EXAMPLE - A embryonic stem cell d2EGFP was established as follows. The target gene encoding enhanced green fluorescent protein (EGFP) was used to establish the stem cell d2EGFP. The d2EGFP expression vector used was pUC19 5', 3' INS24 OCE EGFP. The vector was further inserted with an insulation sequence, a cytomegalovirus (CMV) enhances sequence and an EF-1 alpha sequence inserted to the right side of the BamH I fragment and pd2EGFP 5' INS240 CE was obtained. pd2EGFP 5' INS240 CE was digested using EcoR I and Bsa I and transfected into embryonic stem cell by electroporation method. pd2EGFP embryonic stem cell strain colony was confirmed by the EGFP fluorescence detected using a fluorescence microscope. The embryonic stem cells were cultured by standard methods. Each embryonic stem cell proliferated on the feeder cell was peeled by trypsin-EDTA and cultured in an gelatin coated plate. Then it was transfected using pUC19 5' INS240 EGFP IR having EGFP dsRNA gene containing inverse repeat sequence JP2001046089. A control was built using the plasmid with HPRT (Hypoxanthine phosphoribosyl transferase) dsRNA expression gene (inverse repeat sequence gene). The fluorescence of the cells were analyzed by FACScan. The fluorescence reduction was compared with the control which does not contain the gene. The results showed that the fluorescent reduction of the cell raises 28% compared to the control.(17 pages)

L9 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:417858 HCAPLUS
DOCUMENT NUMBER: 139:1986
TITLE: Facilitation of RNA interference (RNAi) in mammalian cell using invertebrate RNA-dependent RNA polymerase (RdRP) gene family involved in RNAi
INVENTOR(S): Mello, Craig C.; Conte, Darryl, Jr.; Chen, Chun-Chieh
PATENT ASSIGNEE(S): University of Massachusetts, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003044168	A2	20030530	WO 2002-US36725		20021115
WO 2003044168	C2	20040506			
WO 2003044168	A3	20040826			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002360394	A1	20030610	AU 2002-360394		20021115
US 2003114409	A1	20030619	US 2002-295809		20021115
PRIORITY APPLN. INFO.:			US 2001-333811P	P	20011116
			US 2001-331672P	P	20011119
			WO 2002-US36725	W	20021115

AB The present invention features compns. and methods to induce or enhance RNA interference (RNAi) in cells, systems, and organisms using mols. that mediate RNAi in invertebrates such as Caenorhabditis elegans. The invention is based, in part, on the discovery that members of the C. elegans RNA-dependent RNA polymerase (RdRP) gene family, namily ego-1 and rrf-1 genes, are involved in, and can be essential for,

RNAi. Thus, RdRP expression can be used to induce or enhance RNAi in cells, including mammalian cells. RdRP genes can be expressed in combination with one or more of the other genes of the RNAi system, such as Dicer, RDE-1 , or RDE-4.

L9 ANSWER 11 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:770070 SCISEARCH
THE GENUINE ARTICLE: 720HL
TITLE: Transport of dsRNA into cells by the transmembrane protein SID-1
AUTHOR: Feinberg E H; Hunter C P (Reprint)
CORPORATE SOURCE: Harvard Univ, Dept Mol & Cellular Biol, 16 Divin Ave, Cambridge, MA 02138 USA (Reprint); Harvard Univ, Dept Mol & Cellular Biol, Cambridge, MA 02138 USA
COUNTRY OF AUTHOR: USA
SOURCE: SCIENCE, (12 SEP 2003) Vol. 301, No. 5639, pp. 1545-1547. ISSN: 0036-8075.
PUBLISHER: AMER ASSOC ADVANCEMENT SCIENCE, 1200 NEW YORK AVE, NW, WASHINGTON, DC 20005 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 21
ENTRY DATE: Entered STN: 19 Sep 2003
Last Updated on STN: 19 Sep 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB RNA interference (RNAi) spreads systemically in plants and nematodes to silence gene expression distant from the site of initiation. We previously identified a gene, sid-1, essential for systemic but not cell-autonomous RNAi in Caenorhabditis elegans. Here, we demonstrate that SID-1 is a multispan transmembrane protein that sensitizes Drosophila cells to soaking RNAi with a potency that is dependent on double-stranded RNA (dsRNA) length. Further analyses revealed that SID-1 enables passive cellular uptake of dsRNA. These data indicate that systemic RNAi in C. elegans involves SID-1-mediated intercellular transport of dsRNA.

L9 ANSWER 12 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:682305 SCISEARCH
THE GENUINE ARTICLE: 706RN
TITLE: A gene encoding an RNase D exonuclease-like protein is required for post-transcriptional silencing in Arabidopsis
AUTHOR: Glazov E; Phillips K; Budziszewski G J; Meins F (Reprint); Levin J Z
CORPORATE SOURCE: Novartis Res Fdn, Friedrich Miescher Inst Biomed Res, Maulbeerstr 66, CH-4058 Basel, Switzerland (Reprint); Novartis Res Fdn, Friedrich Miescher Inst Biomed Res, CH-4058 Basel, Switzerland; Syngenta Biotechnol Inc, Res Triangle Pk, NC 27709 USA
COUNTRY OF AUTHOR: Switzerland; USA
SOURCE: PLANT JOURNAL, (AUG 2003) Vol. 35, No. 3, pp. 342-349. ISSN: 0960-7412.
PUBLISHER: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 43
ENTRY DATE: Entered STN: 22 Aug 2003
Last Updated on STN: 22 Aug 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Post-transcriptional gene silencing (PTGS) and the closely related phenomenon RNA interference (RNAi) result from the initial

endonucleolytic cleavage of target mRNAs, which are then presumed to be completely hydrolyzed by exoribonucleases. To date, no plant genes required for PTGS are known to encode exoribonucleases. The Arabidopsis Werner Syndrome-like exonuclease (WEX) gene encodes an RNase D domain most similar to that in human Werner Syndrome protein (WRN), but lacks the RecQ helicase domain. It is also related to Caenorhabditis elegans mut-7, which is essential for RNAi, PTGS, and transposon activity. We isolated a loss-of-function mutant, wex-1, that showed greatly reduced expression of WEX mRNA and early flowering. Although wex-1 did not affect expression of a robust marker for transcriptional gene silencing (TGS), PTGS of a green-fluorescent-protein (GFP) reporter gene was blocked in wex-1 and restored by ectopic expression of WEX, indicating that WEX is required for PTGS but not TGS. Thus, members of the RNase D protein family are required for PTGS in both plants and animals. Interestingly, WEX has been shown to interact with an Arabidopsis RecQ helicase, suggesting that these proteins might comprise a functional equivalent of WRN.

L9 ANSWER 13 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:1007849 SCISEARCH
THE GENUINE ARTICLE: 744YQ
TITLE: Transposon silencing in the Caenorhabditis elegans germ line by natural RNAi
AUTHOR: Sijen T; Plasterk R H A (Reprint)
CORPORATE SOURCE: Netherlands Inst Dev Biol, Hubrecht Lab, Uppsalalaan 8, NL-3584 CT Utrecht, Netherlands (Reprint); Netherlands Inst Dev Biol, Hubrecht Lab, NL-3584 CT Utrecht, Netherlands
COUNTRY OF AUTHOR: Netherlands
SOURCE: NATURE, (20 NOV 2003) Vol. 426, No. 6964, pp. 310-314. ISSN: 0028-0836.
PUBLISHER: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 30
ENTRY DATE: Entered STN: 8 Dec 2003
Last Updated on STN: 8 Dec 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Transposable elements are stretches of DNA that can move and multiply within the genome of an organism. The Caenorhabditis elegans genome contains multiple Tc1 transposons that jump in somatic cells, but are silenced in the germ line(1-3). Many mutants that have lost this silencing have also lost the ability to execute RNA interference (RNAi)(2,3), a process whereby genes are suppressed by exposure to homologous double-stranded RNA (dsRNA). Here we show how RNAi causes transposon silencing in the nematode germ line. We find evidence for transposon-derived dsRNAs, in particular to the terminal inverted repeats, and show that these RNAs may derive from read-through transcription of entire transposable elements. Small interfering RNAs of Tc1 were detected. When a germline-expressed reporter gene is fused to a stretch of Tc1 sequence, this transgene is silenced in a manner dependent on functional mutator genes (mut-7, mut-16 and pk732). These results indicate that RNAi surveillance is triggered by fortuitous read-through transcription of dispersed Tc1 copies, which can form dsRNA as a result of 'snap-back' of the terminal inverted repeats. RNAi mediated by this dsRNA silences transposase gene expression.

L9 ANSWER 14 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:596077 SCISEARCH
THE GENUINE ARTICLE: 696HV

TITLE: Gene silencing in Caenorhabditis elegans by transitive RNA interference
AUTHOR: Alder M N; Dames S; Gaudet J; Mango S E (Reprint)
CORPORATE SOURCE: Univ Utah, Huntsmann Canc Inst, 200 Circle Hope, Salt Lake City, UT 84112 USA (Reprint); Univ Utah, Huntsmann Canc Inst, Salt Lake City, UT 84112 USA
COUNTRY OF AUTHOR: USA
SOURCE: RNA-A PUBLICATION OF THE RNA SOCIETY, (JAN 2003) Vol. 9, No. 1, pp. 25-32.
ISSN: 1355-8382.
PUBLISHER: COLD SPRING HARBOR LAB PRESS, PUBLICATIONS DEPT, 500 SUNNYSIDE BLVD, WOODBURY, NY 11797-2924 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 56
ENTRY DATE: Entered STN: 25 Jul 2003
Last Updated on STN: 25 Jul 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB When a cell is exposed to double-stranded RNA (dsRNA), mRNA from the homologous gene is selectively degraded by a process called RNA interference (RNAi). Here, we provide evidence that dsRNA is amplified in Caenorhabditis elegans to ensure a robust RNAi response. Our data suggest a model in which mRNA targeted by RNAi functions as a template for 5' to 3' synthesis of new dsRNA (termed transitive RNAi). Strikingly, the effect is nonautonomous: dsRNA targeted to a gene expressed in one cell type can lead to transitive RNAi-mediated silencing of a second gene expressed in a distinct cell type. These data suggest dsRNA synthesized in vivo can mediate systemic RNAi.

L9 ANSWER 15 OF 25 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2002466218 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12225671
TITLE: PPW-1, a PAZ/PIWI protein required for efficient germline RNAi, is defective in a natural isolate of C. elegans.
AUTHOR: Tijsterman Marcel; Okihara Kristy L; Thijssen Karen; Plasterk Ronald H A
CORPORATE SOURCE: Hubrecht Laboratory, Center for Biomedical Genetics, Uppsalalaan 8, 3584 CT, Utrecht, The Netherlands.
SOURCE: Current biology : CB, (2002 Sep 3) Vol. 12, No. 17, pp. 1535-40.
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 13 Sep 2002
Last Updated on STN: 17 Jun 2003
Entered Medline: 16 Jun 2003

AB One of the remarkable aspects about RNA interference (RNAi) in Caenorhabditis elegans is that the trigger molecules, dsRNA, can be administered via the animal's food. We assayed whether this feature is a universal property of the species by testing numerous strains that have been isolated from different parts of the globe. We found that one isolate from Hawaii had a defect in RNAi that was specific to the germline and was a result of multiple mutations in a PAZ/PIWI domain-containing protein, which we named PPW-1. Deleting ppw-1 in the canonical C. elegans strain Bristol N2 makes it resistant to feeding of dsRNA directed against germline-expressed genes. PPW-1 belongs to the Argonaute family of proteins, which act in posttranscriptional gene silencing and development, and is homologous to the RNAi gene rde-1. Our data indicate that at least two members of

this family are required for complete and effective RNAi in C. elegans.

L9 ANSWER 16 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2002364170 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12110183
TITLE: The dsRNA binding protein RDE-4 interacts with RDE -1, DCR-1, and a DExH-box helicase to direct RNAi in C. elegans.
AUTHOR: Tabara Hiroaki; Yigit Erbay; Siomi Haruhiko; Mello Craig C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Meidcal School, Worcester, MA 1605, USA.
CONTRACT NUMBER: GM58800 (NIGMS)
SOURCE: Cell, (2002 Jun 28) Vol. 109, No. 7, pp. 861-71. Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF480439; GENBANK-AF480440; GENBANK-AY071926
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 12 Jul 2002
Last Updated on STN: 13 Aug 2002
Entered Medline: 12 Aug 2002

AB Double-stranded (ds) RNA induces potent gene silencing, termed RNA interference (RNAi). At an early step in RNAi, an RNaseIII-related enzyme, Dicer (DCR-1), processes long-trigger dsRNA into small interfering RNAs (siRNAs). DCR-1 is also required for processing endogenous regulatory RNAs called miRNAs, but how DCR-1 recognizes its endogenous and foreign substrates is not yet understood. Here we show that the C. elegans RNAi pathway gene, rde-4, encodes a dsRNA binding protein that interacts during RNAi with RNA identical to the trigger dsRNA. RDE-4 protein also interacts in vivo with DCR-1, RDE-1, and a conserved DExH-box helicase. Our findings suggest a model in which RDE-4 and RDE-1 function together to detect and retain foreign dsRNA and to present this dsRNA to DCR-1 for processing.

L9 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:914003 HCAPLUS
DOCUMENT NUMBER: 138:333205
TITLE: RNAi and related mechanisms and their potential use for therapy
AUTHOR(S): Agami, Reuven
CORPORATE SOURCE: Division of Tumor Biology and Center for Biomedical Genetics, The Netherlands Cancer Institute, Amsterdam, 1066 CX, Neth.
SOURCE: Current Opinion in Chemical Biology (2002), 6(6), 829-834
CODEN: COCBF4; ISSN: 1367-5931
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Introduction of double-stranded RNAs into cells can suppress gene expression by mechanisms such as mRNA degradation or inhibition of translation. In mammalian cells, these two responses intersect, a feature that was recently used for the development of novel tools for stable and specific gene inactivation. These new tools were successfully applied to inhibit tumorigenicity and viral replication. Future development of appropriate in vivo delivery systems may make this technol. useful for disease therapy. Introduction of double-stranded RNAs into cells can suppress gene expression. This has recently found application in the development of novel tools for stable and specific gene inactivation. These new tools were successfully applied to inhibit

tumorigenicity and viral replication.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 7
ACCESSION NUMBER: 2002047852 EMBASE
TITLE: RNA helicase mut-14-dependent gene silencing triggered in C. elegans by short antisense RNAs.
AUTHOR: Tijsterman M.; Ketting R.F.; Okihara K.L.; Sijen T.; Plasterk R.H.A.
CORPORATE SOURCE: R.H.A. Plasterk, Hubrecht Laboratory, Uppsalalaan 8, 3584 CT, Utrecht, Netherlands. plasterk@niob.knaw.nl
SOURCE: Science, (25 Jan 2002) Vol. 295, No. 5555, pp. 694-697. .
Refs: 30
ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2002
Last Updated on STN: 14 Feb 2002
AB Posttranscriptional gene silencing in Caenorhabditis elegans results from exposure to double-stranded RNA (dsRNA), a phenomenon designated as RNA interference (RNAi), or from co-suppression, in which transgenic DNA leads to silencing of both the transgene and the endogenous gene. Here we show that single-stranded RNA oligomers of antisense polarity can also be potent inducers of gene silencing. As is the case for co-suppression, antisense RNAs act independently of the RNAi genes rde-1 and rde-4 but require the mutator/ RNAi gene mut-7 and a putative DEAD box RNA helicase, mut-14. Our data favor the hypothesis that gene silencing is accomplished by RNA primer extension using the mRNA as template, leading to dsRNA that is subsequently degraded.

L9 ANSWER 19 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:325987 SCISEARCH
THE GENUINE ARTICLE: 537ZC
TITLE: Fertile hypomorphic ARGONAUTE (ago1) mutants impaired in post-transcriptional gene silencing and virus resistance
AUTHOR: Morel J B; Godon C; Mourrain P; Beclin C; Boutet S; Feuerbach F; Proux F; Vaucheret H (Reprint)
CORPORATE SOURCE: INRA, Biol Cellulaire Lab, F-78026 Versailles, France (Reprint)
COUNTRY OF AUTHOR: France
SOURCE: PLANT CELL, (MAR 2002) Vol. 14, No. 3, pp. 629-639.
ISSN: 1040-4651.
PUBLISHER: AMER SOC PLANT BIOLOGISTS, 15501 MONONA DRIVE, ROCKVILLE, MD 20855 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 44
ENTRY DATE: Entered STN: 26 Apr 2002
Last Updated on STN: 26 Apr 2002
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Transgene-induced post-transcriptional gene silencing (PTGS) results from specific degradation of RNAs that are homologous with the transgene transcribed sequence. This phenomenon, also known as cosuppression in plants and quelling in fungi, resembles RNA interference (RNAi) in animals. Indeed, cosuppression/quelling/RNAi require related PAZ/PIWI proteins (AGO1/QDE-2/RDE-1), indicating that these mechanisms are related. Unlike Neurospora crassa qde-2 and

Caenorhabditis elegans rde-1 mutants, which are morphologically normal, the 24 known Arabidopsis ago1 mutants display severe developmental abnormalities and are sterile. Here, we report the isolation of hypomorphic ago I mutants, including fertile ones. We show that these hypomorphic ago1 mutants are defective for PTGS, like null sgs2, sgs3, and ago1 mutants, suggesting that PTGS is more sensitive than development to perturbations in AGO1. Conversely, a mutation in ZWILLE/PINHEAD, another member of the Arabidopsis AGO1 gene family, affects development but not PTGS. Similarly, mutations in ALG-1 and ALG-2, two members of the C. elegans RDE-1 gene family, affect development but not RNAi, indicating that the control of PTGS/RNAi and development by PAZ/PIWI proteins can be uncoupled. Finally, we show that hypomorphic ago1 mutants are hypersensitive to virus infection, confirming the hypothesis that in plants PTGS is a mechanism of defense against viruses.

L9 ANSWER 20 OF 25 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2002120843 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11835276
TITLE: Control of developmental timing by small temporal RNAs: a paradigm for RNA-mediated regulation of gene expression.
AUTHOR: Banerjee Diya; Slack Frank
CORPORATE SOURCE: Department of Molecular, Cellular and Development Biology, Yale University, 266 Whitney Ave., New Haven, CT 06520, USA.
SOURCE: BioEssays : news and reviews in molecular, cellular and developmental biology, (2002 Feb) Vol. 24, No. 2, pp. 119-29. Ref: 61
Journal code: 8510851. ISSN: 0265-9247.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 22 Feb 2002
Last Updated on STN: 2 Jul 2002
Entered Medline: 1 Jul 2002
AB Heterochronic genes control the timing of developmental programs. In C. elegans, two key genes in the heterochronic pathway, lin-4 and let-7, encode small temporally expressed RNAs (stRNAs) that are not translated into protein. These stRNAs exert negative post-transcriptional regulation by binding to complementary sequences in the 3' untranslated regions of their target genes. stRNAs are transcribed as longer precursor RNAs that are processed by the RNase Dicer/DCR-1 and members of the RDE-1/AGO1 family of proteins, which are better known for their roles in RNA interference (RNAi). However, stRNA function appears unrelated to RNAi. Both sequence and temporal regulation of let-7 stRNA is conserved in other animal species suggesting that this is an evolutionarily ancient gene. Indeed, C. elegans, Drosophila and humans encode at least 86 other RNAs with similar structural features to lin-4 and let-7. We postulate that other small non-coding RNAs may function as stRNAs to control temporal identity during development in C. elegans and other organisms.

L9 ANSWER 21 OF 25 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2001412025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11461699
TITLE: Genes and mechanisms related to RNA interference regulate expression of the small temporal RNAs that control C. elegans developmental timing.
AUTHOR: Grishok A; Pasquinelli A E; Conte D; Li N; Parrish S; Ha I;

Baillie D L; Fire A; Ruvkun G; Mello C C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA.
CONTRACT NUMBER: GM07321 (NIGMS)
GM37706 (NIGMS)
GM58800 (NIGMS)
SOURCE: Cell, (2001 Jul 13) Vol. 106, No. 1, pp. 23-34.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 13 Aug 2001
Last Updated on STN: 13 Aug 2001
Entered Medline: 9 Aug 2001

AB RNAi is a gene-silencing phenomenon triggered by double-stranded (ds) RNA and involves the generation of 21 to 26 nt RNA segments that guide mRNA destruction. In Caenorhabditis elegans, lin-4 and let-7 encode small temporal RNAs (stRNAs) of 22 nt that regulate stage-specific development. Here we show that inactivation of genes related to RNAi pathway genes, a homolog of Drosophila Dicer (dcr-1), and two homologs of rde-1 (alg-1 and alg-2), cause heterochronic phenotypes similar to lin-4 and let-7 mutations. Further we show that dcr-1, alg-1, and alg-2 are necessary for the maturation and activity of the lin-4 and let-7 stRNAs. Our findings suggest that a common processing machinery generates guide RNAs that mediate both RNAi and endogenous gene regulation.

L9 ANSWER 22 OF 25 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2001022703 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11016954
TITLE: AGO1, QDE-2, and RDE-1 are related proteins required for post-transcriptional gene silencing in plants, quelling in fungi, and RNA interference in animals.
AUTHOR: Fagard M; Boutet S; Morel J B; Bellini C; Vaucheret H
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, Institut National de la Recherche Agronomique, 78026 Versailles Cedex, France.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2000 Oct 10) Vol. 97, No. 21, pp. 11650-4.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 9 Nov 2000

AB Introduction of transgene DNA may lead to specific degradation of RNAs that are homologous to the transgene transcribed sequence through phenomena named post-transcriptional gene silencing (PTGS) in plants, quelling in fungi, and RNA interference (RNAi) in animals. It was shown previously that PTGS, quelling, and RNAi require a set of related proteins (SGS2, QDE-1, and EGO-1, respectively). Here we report the isolation of Arabidopsis mutants impaired in PTGS which are affected at the Argonaute1 (AGO1) locus. AGO1 is similar to QDE-2 required for quelling and RDE-1 required for RNAi. Sequencing of ago1 mutants revealed one amino acid essential for PTGS that is also present in QDE-2 and RDE-1 in a highly conserved motif. Taken together, these results confirm the hypothesis that these processes derive from a common ancestral

mechanism that controls expression of invading nucleic acid molecules at the post-transcriptional level. As opposed to rde-1 and qde-2 mutants, which are viable, ago1 mutants display several developmental abnormalities, including sterility. These results raise the possibility that PTGS, or at least some of its elements, could participate in the regulation of gene expression during development in plants.

L9 ANSWER 23 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2000123929 EMBASE
TITLE: Genetic requirements for inheritance of RNAi in C. elegans.
AUTHOR: Grishok A.; Tabara H.; Mello C.C.
CORPORATE SOURCE: C.C. Mello, Program in Molecular Medicine, Department of Cell Biology, Univ. of Massachusetts Cancer Center, 373 Plantation Street, Worcester, MA 01605, United States. craig.mello@ummed.edu
SOURCE: Science, (31 Mar 2000) Vol. 287, No. 5462, pp. 2494-2497. . ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000

AB In Caenorhabditis elegans, the introduction of double-stranded RNA triggers sequence-specific genetic interference (RNAi) that is transmitted to offspring. The inheritance properties associated with this phenomenon were examined. Transmission of the interference effect occurred through a dominant extragenic agent. The wild-type activities of the RNAi pathway genes rde-1 and rde-4 were required for the formation of this interfering agent but were not needed for interference thereafter. In contrast, the rde-2 and mut-7 genes were required downstream for interference. These findings provide evidence for germ line transmission of an extragenic sequence-specific silencing factor and implicate rde-1 and rde-4 in the formation of the inherited agent.

L9 ANSWER 24 OF 25 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:535206 SCISEARCH
THE GENUINE ARTICLE: 333TC
TITLE: Transgene-mediated cosuppression in the C-elegans germ line
AUTHOR: Dernburg A F; Zalevsky J; Colaiacovo M P; Villeneuve A M (Reprint)
CORPORATE SOURCE: Stanford Univ, Sch Med, Dept Dev Biol, Stanford, CA 94305 USA (Reprint); Stanford Univ, Sch Med, Dept Genet, Stanford, CA 94305 USA
COUNTRY OF AUTHOR: USA
SOURCE: GENES & DEVELOPMENT, (1 JUL 2000) Vol. 14, No. 13, pp. 1578-1583.
ISSN: 0890-9369.
PUBLISHER: COLD SPRING HARBOR LAB PRESS, 1 BUNGTOWN RD, PLAINVIEW, NY 11724 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 40
ENTRY DATE: Entered STN: 2000
Last Updated on STN: 2000
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Functional silencing of chromosomal loci can be induced by transgenes

(cosuppression) or by introduction of double-stranded RNA (RNAi). Here, we demonstrate the generality of and define rules for a transgene-mediated cosuppression phenomenon in the Caenorhabditis elegans germ line. Functional repression is not a consequence of persistent physical association between transgenes and endogenous genes or of mutations in affected genes. The cosuppression mechanism likely involves an RNA mediator that defines its target specificity, reminiscent of RNAi. Cosuppression is strongly abrogated in rde-2 and mut-7 mutants, but is not blocked in an rde-1 mutant, indicating that cosuppression and RNAi have overlapping but distinct genetic requirements.

L9 ANSWER 25 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 11

ACCESSION NUMBER: 1999365904 EMBASE
TITLE: The rde-1 gene, RNA interference, and transposon silencing in C. elegans.
AUTHOR: Tabara H.; Sarkissian M.; Kelly W.G.; Fleenor J.; Grishok A.; Timmons L.; Fire A.; Mello C.C.
CORPORATE SOURCE: H. Tabara, Department of Cell Biology, Program in Molecular Medicine, Univ. of Massachusetts Cancer Center, Worcester, MA 01605, United States. craig.mello@ummed.edu
SOURCE: Cell, (1999) Vol. 99, No. 2, pp. 123-132. .
Refs: 57
ISSN: 0092-8674 CODEN: CELLB5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Nov 1999
Last Updated on STN: 4 Nov 1999

AB Double-stranded (ds) RNA can induce sequence-specific inhibition of gene function in several organisms. However, both the mechanism and the physiological role of the interference process remain mysterious. In order to study the interference process, we have selected C. elegans mutants resistant to dsRNA-mediated interference (RNAi). Two loci, rde-1 and rde-4, are defined by mutants strongly resistant to RNAi but with no obvious defects in growth or development. We show that rde-1 is a member of the piwi/sting/argonaute/zwille/elF2C gene family conserved from plants to vertebrates. Interestingly, several, but not all, RNAi -deficient strains exhibit mobilization of the endogenous transposons. We discuss implications for the mechanism of RNAi and the possibility that one natural function of RNAi is transposon silencing.

=> d his

(FILE 'HOME' ENTERED AT 09:14:20 ON 17 AUG 2006)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:14:51 ON 17 AUG 2006

L1 167 S "RDE-1" OR "RDE 1"
L2 19880 S RNAI
L3 131 S L1 AND L2
L4 444660 S INTERFERENCE
L5 116 S L3 AND L4
L6 41 DUP REM L5 (75 DUPLICATES REMOVED)
L7 7844066 S CLON? OR EXPRESS? OR RECOMBINANT
L8 56 S L3 AND L7
L9 25 DUP REM L8 (31 DUPLICATES REMOVED)

```
=> e mello G c /au
E1            7     MELLO G B/AU
E2            1     MELLO G B D/AU
E3            6 --> MELLO G C/AU
E4            1     MELLO G C R O T/AU
E5            2     MELLO G F P/AU
E6            2     MELLO G J P/AU
E7            2     MELLO G K/AU
E8            5     MELLO G P S/AU
E9            1     MELLO G S/AU
E10           1     MELLO G S B/AU
E11           2     MELLO G W/AU
E12           1     MELLO GILBERTO A/AU

=> s e3
L10           6 "MELLO G C"/AU

=> e fire a/au
E1            1     FIRDUS NEDZAD/AU
E2            2     FIRE/AU
E3          288 --> FIRE A/AU
E4            1     FIRE A */AU
E5           10     FIRE A Z/AU
E6          134     FIRE ANDREW/AU
E7            8     FIRE ANDREW Z/AU
E8            1     FIRE ANDY/AU
E9            1     FIRE C/AU
E10           2     FIRE D/AU
E11          23     FIRE E/AU
E12          11     FIRE ELLA/AU

=> s e3-e7
L11         441 ("FIRE A"/AU OR "FIRE A *"/AU OR "FIRE A Z"/AU OR "FIRE ANDREW"/
                AU OR "FIRE ANDREW Z"/AU)

=> e tabara h/au
E1            1     TABARA DAVID/AU
E2            5     TABARA ELEONORA/AU
E3          124 --> TABARA H/AU
E4           14     TABARA HIDEKI/AU
E5           30     TABARA HIROAKI/AU
E6            1     TABARA HIROKAI/AU
E7            7     TABARA HIROTO/AU
E8            1     TABARA HISAO/AU
E9            1     TABARA I/AU
E10           2     TABARA ISAO/AU
E11           1     TABARA ISTVAN/AU
E12           7     TABARA J/AU

=> s e3-e6
L12         169 ("TABARA H"/AU OR "TABARA HIDEKI"/AU OR "TABARA HIROAKI"/AU OR
                "TABARA HIROKAI"/AU)

=> e grishok a/au
E1            1     GRISHNYAK V G/AU
E2            2     GRISHNYAKOV S B/AU
E3           36 --> GRISHOK A/AU
E4            2     GRISHOK A A/AU
E5           27     GRISHOK ALLA/AU
E6            2     GRISHOK L P/AU
E7            1     GRISHOLD W/AU
E8            3     GRISHOM J/AU
E9            2     GRISHOV F I/AU
E10           1     GRISHOV VALERIJ A/AU
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E11           9     GRISHOVA A I/AU
E12           1     GRISHOVA A N/AU

=> s e3
L13          36 "GRISHOK A"/AU

=> d his

     (FILE 'HOME' ENTERED AT 09:14:20 ON 17 AUG 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:14:51 ON 17 AUG 2006
L1           167 S "RDE-1" OR "RDE 1"
L2         19880 S RNAI
L3           131 S L1 AND L2
L4        444660 S INTERFERENCE
L5           116 S L3 AND L4
L6            41 DUP REM L5 (75 DUPLICATES REMOVED)
L7       7844066 S CLON? OR EXPRESS? OR RECOMBINANT
L8            56 S L3 AND L7
L9            25 DUP REM L8 (31 DUPLICATES REMOVED)
                 E MELLO G C /AU
L10            6 S E3
                 E FIRE A/AU
L11          441 S E3-E7
                 E TABARA H/AU
L12          169 S E3-E6
                 E GRISHOK A/AU
L13           36 S E3

=> s l10 or l11 or l12 or l13
L14         620 L10 OR L11 OR L12 OR L13

=> s l3 and l14
L15          39 L3 AND L14

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16           10 DUP REM L15 (29 DUPLICATES REMOVED)

=> d 1-10 ibib ab

L16  ANSWER 1 OF 10  EMBASE  COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN                                      DUPLICATE 1
ACCESSION NUMBER:   2005134753  EMBASE
TITLE:              Transcriptional silencing of a transgene by RNAi
                    in the soma of C. elegans.
AUTHOR:             Grishok A.; Sinskey J.L.; Sharp P.A.
CORPORATE SOURCE:   P.A. Sharp, Center for Cancer Research, MA Institute of
                    Technology, Cambridge, MA 02139, United States.
                    sharppa@mit.edu
SOURCE:             Genes and Development, (5 Mar 2005) Vol. 19, No. 6, pp.
                    683-696. .
                    Refs: 59
                    ISSN: 0890-9369  CODEN: GEDEEP
COUNTRY:            United States
DOCUMENT TYPE:      Journal; Article
FILE SEGMENT:       004     Microbiology
LANGUAGE:           English
SUMMARY LANGUAGE:   English
ENTRY DATE:         Entered STN: 7 Apr 2005
                    Last Updated on STN: 7 Apr 2005
AB   The silencing of transgene expression at the level of transcription in the
     soma of Caenorhabditis elegans through an RNAi-dependent pathway
```

has not been previously characterized. Most gene silencing due to RNAi in C. elegans occurs at the post-transcriptional level. We observed transcriptional silencing when worms containing the elt-2::gfp/LacZ transgene were fed RNA produced from the commonly used L4440 vector. The transgene and the vector share plasmid backbone sequences. This transgene silencing depends on multiple RNAi pathway genes, including dcr-1, rde-1, rde-4, and rrf-1. Unlike post-transcriptional gene silencing in worms, elt-2::gfp/lacZ silencing is dependent on the PAZ-PIWI protein Alg-1 and on the HP1 homolog Hpl-2. The latter is a chromatin silencing factor, and expression of the transgene is inhibited at the level of intron-containing precursor mRNA. This inhibition is accompanied by a decrease in the acetylation of histones associated with the transgene. This transcriptional silencing in the soma can be distinguished from transgene silencing in the germline by its inability to be transmitted across generations and its dependence on the rde-1 gene. We therefore define this type of silencing as RNAi-induced Transcriptional Gene Silencing (RNAi-TGS). Additional chromatin-modifying components affecting RNAi-TGS were identified in a candidate RNAi screen. .COPYRGT. 2005 by Cold Spring Harbor Laboratory Press.

L16 ANSWER 2 OF 10 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:229753 SCISEARCH
THE GENUINE ARTICLE: 901FC
TITLE: A member of the polymerase beta nucleotidyltransferase superfamily is required for RNA interference in C-elegans
AUTHOR: Chen C C G; Simard M J; Tabara H; Brownell D R; McCollough J A; Mello C C (Reprint)
CORPORATE SOURCE: Univ Massachusetts, Sch Med, Program Mol Med, Worcester, MA 01605 USA (Reprint); Univ Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester, MA 01605 USA; Kyoto Univ, HMRO, Grad Sch Med, Kyoto 6068501, Japan craig.mello@umassmed.edu
COUNTRY OF AUTHOR: USA; Japan
SOURCE: CURRENT BIOLOGY, (22 FEB 2005) Vol. 15, No. 4, pp. 378-383 .
ISSN: 0960-9822.
PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 20
ENTRY DATE: Entered STN: 10 Mar 2005
Last Updated on STN: 10 Mar 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB RNA interference (RNAi) is an ancient, highly conserved mechanism in which small RNA molecules (siRNAs) guide the sequence-specific silencing of gene expression [1]. Several silencing machinery protein components have been identified, including helicases, RNase-related proteins, double- and singlestranded RNA binding proteins, and RNA-dependent RNA polymerase-related proteins [2]. Work on these factors has led to the revelation that RNAi mechanisms intersect with cellular pathways required for development and fertility (3, 4]. Despite rapid progress in understanding key steps in the RNAi pathway, it is clear that many factors required for both RNAi and related developmental mechanisms have not yet been identified. Here, we report the characterization of the C. elegans gene rde-3. Genetic analysis of presumptive null alleles indicates that rde-3 is required for siRNA accumulation and for efficient RNAi in all tissues, and it is essential for fertility and viability at high temperatures. RDE-3 contains conserved domains found in the polymerase beta nucleotidyltransferase superfamily, which includes conventional poly(A)

polymerases, 2'-5' oligoadenylate synthetase (OAS), and yeast Trf4p [5]. These findings implicate a new enzymatic modality in RNAi and suggest possible models for the role of RDE-3 in the RNAi mechanism.

L16 ANSWER 3 OF 10 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005027594 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15653635
TITLE: RDE-2 interacts with MUT-7 to mediate RNA interference in Caenorhabditis elegans.
AUTHOR: Tops Bastiaan B J; Tabara Hiroaki; Sijen Titia; Simmer Femke; Mello Craig C; Plasterk Ronald H A; Ketting Rene F
CORPORATE SOURCE: Hubrecht Laboratory, Centre for Biomedical Genetics Uppsalalaan 8, 3584 CT Utrecht, The Netherlands.
SOURCE: Nucleic acids research, (2005) Vol. 33, No. 1, pp. 347-55. Electronic Publication: 2005-01-13. Journal code: 0411011. E-ISSN: 1362-4962.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 19 Jan 2005
Last Updated on STN: 11 Feb 2005
Entered Medline: 10 Feb 2005
AB In Caenorhabditis elegans, the activity of transposable elements is repressed in the germline. One of the mechanisms involved in this repression is RNA interference (RNAi), a process in which dsRNA targets cleavage of mRNAs in a sequence-specific manner. The first gene found to be involved in RNAi and transposon silencing in C.elegans is mut-7, a gene encoding a putative exoribonuclease. Here, we show that the MUT-7 protein resides in complexes of approximately 250 kDa in the nucleus and in the cytosol. In addition, we find that upon triggering of RNAi the cytosolic MUT-7 complex increases in size. This increase is independent of the presence of target RNA, but does depend on the presence of RDE-1 and RDE-4, two proteins involved in small interfering RNA (siRNA) production. Finally, using a yeast two-hybrid screen, we identified RDE-2/MUT-8 as one of the other components of this complex. This protein is encoded by the rde-2/mut-8 locus, previously implicated in RNAi and transposon silencing. Using genetic complementation analysis, we show that the interaction between these two proteins is required for efficient RNAi in vivo. Together these data support a role for the MUT-7/RDE-2 complex downstream of siRNA formation, but upstream of siRNA mediated target RNA recognition, possibly indicating a role in the siRNA amplification step.

L16 ANSWER 4 OF 10 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002364170 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12110183
TITLE: The dsRNA binding protein RDE-4 interacts with RDE -1, DCR-1, and a DExH-box helicase to direct RNAi in C. elegans.
AUTHOR: Tabara Hiroaki; Yigit Erbay; Siomi Haruhiko; Mello Craig C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Meidcal School, Worcester, MA 1605, USA.
CONTRACT NUMBER: GM58800 (NIGMS)
SOURCE: Cell, (2002 Jun 28) Vol. 109, No. 7, pp. 861-71. Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF480439; GENBANK-AF480440; GENBANK-AY071926
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 12 Jul 2002
Last Updated on STN: 13 Aug 2002
Entered Medline: 12 Aug 2002

AB Double-stranded (ds) RNA induces potent gene silencing, termed RNA interference (RNAi). At an early step in RNAi, an RNaseIII-related enzyme, Dicer (DCR-1), processes long-trigger dsRNA into small interfering RNAs (siRNAs). DCR-1 is also required for processing endogenous regulatory RNAs called miRNAs, but how DCR-1 recognizes its endogenous and foreign substrates is not yet understood. Here we show that the C. elegans RNAi pathway gene, rde-4, encodes a dsRNA binding protein that interacts during RNAi with RNA identical to the trigger dsRNA. RDE-4 protein also interacts in vivo with DCR-1, RDE-1, and a conserved DExH-box helicase. Our findings suggest a model in which RDE-4 and RDE-1 function together to detect and retain foreign dsRNA and to present this dsRNA to DCR-1 for processing.

L16 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:300734 HCAPLUS
DOCUMENT NUMBER: 134:321556
TITLE: RNA interference pathway genes as tools for targeted genetic interference
INVENTOR(S): Mello, Craig C.; Fire, Andrew; Tabara, Hiroaki; Grishok, Alla
PATENT ASSIGNEE(S): University of Massachusetts, USA; Carnegie Institution of Washington
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001029058	A1	20010426	WO 2000-US28470	20001013
W: AU, CA, JP, KR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2386270	AA	20010426	CA 2000-2386270	20001013
AU 2001010865	A5	20010430	AU 2001-10865	20001013
EP 1235842	A1	20020904	EP 2000-972167	20001013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
JP 2003516124	T2	20030513	JP 2001-531856	20001013
US 2004265839	A1	20041230	US 2003-645746	20030820
US 2005100913	A1	20050512	US 2003-645735	20030820
US 2006024798	A1	20060202	US 2005-144985	20050603
AU 2006201716	A1	20060525	AU 2006-201716	20060426

PRIORITY APPLN. INFO.:	US 1999-159776P	P	19991015
	US 2000-193218P	P	20000330
	AU 2001-10865	A3	20001013
	US 2000-689992	A3	20001013
	WO 2000-US28470	W	20001013

AB Genes involved in double-stranded RNA interference (RNAi pathway genes) are identified and used to investigate the RNAi pathway. RNAi pathway components provide activities necessary for double-stranded RNA-dependent gene silencing (genetic interference). Genes RDE-1 and RDE-4 were identified using screens for Caenorhabditis elegans strains mutant for RNAi, and the mutations are further characterized for germline and somatic effects,

effects on transposon mobilization, X chromosome loss and transgene silencing, and target tissue activity. The genes and their products are also useful for modulating RNAi pathway activity.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 10 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001574258 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11680844
TITLE: Distinct roles for RDE-1 and RDE-4 during RNA interference in Caenorhabditis elegans.
AUTHOR: Parrish S; Fire A
CORPORATE SOURCE: Department of Embryology, Carnegie Institution of Washington, Baltimore, Maryland 21210, USA.
CONTRACT NUMBER: GM07231 (NIGMS)
GM37706 (NIGMS)
SOURCE: RNA (New York, N.Y.), (2001 Oct) Vol. 7, No. 10, pp. 1397-402.
Journal code: 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 30 Oct 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 4 Dec 2001

AB RNA interference (RNAi) is a cellular defense mechanism that uses double-stranded RNA (dsRNA) as a sequence-specific trigger to guide the degradation of homologous single-stranded RNAs. RNAi is a multistep process involving several proteins and at least one type of RNA intermediate, a population of small 21-25 nt RNAs (called siRNAs) that are initially derived from cleavage of the dsRNA trigger. Genetic screens in Caenorhabditis elegans have identified numerous mutations that cause partial or complete loss of RNAi. In this work, we analyzed cleavage of injected dsRNA to produce the initial siRNA population in animals mutant for rde-1 and rde-4, two genes that are essential for RNAi but that are not required for organismal viability or fertility. Our results suggest distinct roles for RDE-1 and RDE-4 in the interference process. Although null mutants lacking rde-1 show no phenotypic response to dsRNA, the amount of siRNAs generated from an injected dsRNA trigger was comparable to that of wild-type. By contrast, mutations in rde-4 substantially reduced the population of siRNAs derived from an injected dsRNA trigger. Injection of chemically synthesized 24- or 25-nt siRNAs could circumvent RNAi resistance in rde-4 mutants, whereas no bypass was observed in rde-1 mutants. These results support a model in which RDE-4 is involved before or during production of siRNAs, whereas RDE-1 acts after the siRNAs have been formed.

L16 ANSWER 7 OF 10 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001412025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11461699
TITLE: Genes and mechanisms related to RNA interference regulate expression of the small temporal RNAs that control C. elegans developmental timing.
AUTHOR: Grishok A; Pasquinelli A E; Conte D; Li N; Parrish S; Ha I; Baillie D L; Fire A; Ruvkun G; Mello C C
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA.
CONTRACT NUMBER: GM07321 (NIGMS)
GM37706 (NIGMS)

GM58800 (NIGMS)
SOURCE: Cell, (2001 Jul 13) Vol. 106, No. 1, pp. 23-34.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 13 Aug 2001
Last Updated on STN: 13 Aug 2001
Entered Medline: 9 Aug 2001

AB RNAi is a gene-silencing phenomenon triggered by double-stranded (ds) RNA and involves the generation of 21 to 26 nt RNA segments that guide mRNA destruction. In Caenorhabditis elegans, lin-4 and let-7 encode small temporal RNAs (stRNAs) of 22 nt that regulate stage-specific development. Here we show that inactivation of genes related to RNAi pathway genes, a homolog of Drosophila Dicer (dcr-1), and two homologs of rde-1 (alg-1 and alg-2), cause heterochronic phenotypes similar to lin-4 and let-7 mutations. Further we show that dcr-1, alg-1, and alg-2 are necessary for the maturation and activity of the lin-4 and let-7 stRNAs. Our findings suggest that a common processing machinery generates guide RNAs that mediate both RNAi and endogenous gene regulation.

L16 ANSWER 8 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2000207007 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10741970
TITLE: Genetic requirements for inheritance of RNAi in C. elegans.
AUTHOR: Grishok A; Tabara H; Mello C C
CORPORATE SOURCE: Program in Molecular Medicine, Department of Cell Biology, University of Massachusetts Cancer Center, Two Biotech Suite 213, 373 Plantation Street, Worcester, MA 01605, USA.
CONTRACT NUMBER: GM58800 (NIGMS)
SOURCE: Science, (2000 Mar 31) Vol. 287, No. 5462, pp. 2494-7.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000
Entered Medline: 11 Apr 2000

AB In Caenorhabditis elegans, the introduction of double-stranded RNA triggers sequence-specific genetic interference (RNAi) that is transmitted to offspring. The inheritance properties associated with this phenomenon were examined. Transmission of the interference effect occurred through a dominant extragenic agent. The wild-type activities of the RNAi pathway genes rde-1 and rde-4 were required for the formation of this interfering agent but were not needed for interference thereafter. In contrast, the rde-2 and mut-7 genes were required downstream for interference. These findings provide evidence for germ line transmission of an extragenic sequence-specific silencing factor and implicate rde-1 and rde-4 in the formation of the inherited agent.

L16 ANSWER 9 OF 10 EMBASE DUPLICATE 6
ACCESSION NUMBER: 2000123929 EMBASE
TITLE: Genetic requirements for inheritance of RNAi in C. elegans.
AUTHOR: Grishok A.; Tabara H.; Mello C.C.

CORPORATE SOURCE: C.C. Mello, Program in Molecular Medicine, Department of Cell Biology, Univ. of Massachusetts Cancer Center, 373 Plantation Street, Worcester, MA 01605, United States. craig.mello@ummed.edu
SOURCE: Science, (31 Mar 2000) Vol. 287, No. 5462, pp. 2494-2497. . ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 21 Apr 2000
Last Updated on STN: 21 Apr 2000

AB In Caenorhabditis elegans, the introduction of double-stranded RNA triggers sequence-specific genetic interference (RNAi) that is transmitted to offspring. The inheritance properties associated with this phenomenon were examined. Transmission of the interference effect occurred through a dominant extragenic agent. The wild-type activities of the RNAi pathway genes rde-1 and rde-4 were required for the formation of this interfering agent but were not needed for interference thereafter. In contrast, the rde-2 and mut-7 genes were required downstream for interference. These findings provide evidence for germ line transmission of an extragenic sequence-specific silencing factor and implicate rde-1 and rde-4 in the formation of the inherited agent.

L16 ANSWER 10 OF 10 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000004389 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10535731
TITLE: The rde-1 gene, RNA interference, and transposon silencing in C. elegans.
AUTHOR: Tabara H; Sarkissian M; Kelly W G; Fleenor J; Grishok A; Timmons L; Fire A; Mello C C
CORPORATE SOURCE: Department of Cell Biology, Program in Molecular Medicine, University of Massachusetts Cancer Center, Worcester 01605, USA.
CONTRACT NUMBER: GM37706 (NIGMS)
GM58800 (NIGMS)
HD08353 (NICHD)
SOURCE: Cell, (1999 Oct 15) Vol. 99, No. 2, pp. 123-32. Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF180730
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 10 Nov 1999

AB Double-stranded (ds) RNA can induce sequence-specific inhibition of gene function in several organisms. However, both the mechanism and the physiological role of the interference process remain mysterious. In order to study the interference process, we have selected C. elegans mutants resistant to dsRNA-mediated interference (RNAi). Two loci, rde-1 and rde-4, are defined by mutants strongly resistant to RNAi but with no obvious defects in growth or development. We show that rde-1 is a member of the piwi/sting/argonaute/zwille/eIF2C gene family conserved from plants to vertebrates. Interestingly, several, but not all, RNAi -deficient strains exhibit mobilization of the endogenous transposons. We discuss implications for the mechanism of RNAi and the possibility that one natural function of RNAi is transposon silencing.

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=> d his

     (FILE 'HOME' ENTERED AT 09:14:20 ON 17 AUG 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:14:51 ON 17 AUG 2006
L1           167 S "RDE-1" OR "RDE 1"
L2         19880 S RNAI
L3           131 S L1 AND L2
L4        444660 S INTERFERENCE
L5           116 S L3 AND L4
L6            41 DUP REM L5 (75 DUPLICATES REMOVED)
L7       7844066 S CLON? OR EXPRESS? OR RECOMBINANT
L8            56 S L3 AND L7
L9            25 DUP REM L8 (31 DUPLICATES REMOVED)
                 E MELLO G C /AU
L10            6 S E3
                 E FIRE A/AU
L11          441 S E3-E7
                 E TABARA H/AU
L12          169 S E3-E6
                 E GRISHOK A/AU
L13           36 S E3
L14          620 S L10 OR L11 OR L12 OR L13
L15           39 S L3 AND L14
L16           10 DUP REM L15 (29 DUPLICATES REMOVED)
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1	L1	123	"RDE-1" or "rde 1"
2	L2	3598	RNAi
3	L3	100	l1 same l2
4	L4	135065	clon? or express? or recombinant
5	L5	18	l3 same l4
6	L6	149471	TABARA MELLO GRISHOK FIRE
7	L7	18	l3 and l5

	Issue Date	Pages	Document ID	Title
1	20060713	46	US 20060154237 A1	Soluble rna polymerase protein and methods for the use thereof
2	20060209	13	US 20060030003 A1	Composition and method for introduction of RNA interference sequences into targeted cells and tissues
3	20060202	62	US 20060024798 A1	RNA interference pathway genes as tools for targeted genetic interference
4	20051201	87	US 20050266552 A1	Reagents and methods for identification of RNAi pathway genes and chemical modulators of RNAi
5	20051124	134	US 20050260652 A1	Compositions and methods that modulate RNA interference
6	20051117	116	US 20050255487 A1	Methods and compositions for selecting siRNA of improved functionality
7	20051103	102	US 20050246794 A1	Functional and hyperfunctional siRNA
8	20051103	126	US 20050245475 A1	Functional and hyperfunctional siRNA directed against Bcl-2
9	20051006	107	US 20050223427 A1	Modified polynucleotides for reducing off-target effects in RNA interference
10	20050915	159	US 20050203043 A1	Identification of toxic nucleotide sequences

11	20050512	61	US 2005010091 3 A1	RNA interference pathway genes as tools for targeted genetic interference

	Issue Date	Pages	Document ID	Title
12	20050217	141	US 20050037387 A1	Modulation of the RNA interference pathway
13	20050106	26	US 20050003541 A1	ES cells having enhanced RNAi effect
14	20041230	159	US 20040266707 A1	Stabilized polynucleotides for use in RNA interference
15	20041230	61	US 20040265839 A1	RNA interference pathway genes as tools for targeted genetic interference
16	20041111	57	US 20040224405 A1	siRNA induced systemic gene silencing in mammalian systems
17	20041007	66	US 20040198640 A1	Stabilized polynucleotides for use in RNA interference
18	20030619	22	US 20030114409 A1	Facilitation of RNA interference

	Issue Date	Pages	Document ID	Title
1	20060713	46	US 20060154237 A1	Soluble rna polymerase protein and methods for the use thereof
2	20060209	13	US 20060030003 A1	Composition and method for introduction of RNA interference sequences into targeted cells and tissues
3	20060202	62	US 20060024798 A1	RNA interference pathway genes as tools for targeted genetic interference
4	20051201	87	US 20050266552 A1	Reagents and methods for identification of RNAi pathway genes and chemical modulators of RNAi
5	20051124	134	US 20050260652 A1	Compositions and methods that modulate RNA interference
6	20051117	116	US 20050255487 A1	Methods and compositions for selecting siRNA of improved functionality
7	20051103	102	US 20050246794 A1	Functional and hyperfunctional siRNA
8	20051103	126	US 20050245475 A1	Functional and hyperfunctional siRNA directed against Bcl-2
9	20051006	107	US 20050223427 A1	Modified polynucleotides for reducing off-target effects in RNA interference
10	20050915	159	US 20050203043 A1	Identification of toxic nucleotide sequences

11	20050512	61	US 20050100913 A1	RNA interference pathway genes as tools for targeted genetic interference

	Issue Date	Pages	Document ID	Title
12	20050217	141	US 20050037387 A1	Modulation of the RNA interference pathway
13	20050106	26	US 20050003541 A1	ES cells having enhanced RNAi effect
14	20041230	159	US 20040266707 A1	Stabilized polynucleotides for use in RNA interference
15	20041230	61	US 20040265839 A1	RNA interference pathway genes as tools for targeted genetic interference
16	20041111	57	US 20040224405 A1	siRNA induced systemic gene silencing in mammalian systems
17	20041007	66	US 20040198640 A1	Stabilized polynucleotides for use in RNA interference
18	20030619	22	US 20030114409 A1	Facilitation of RNA interference